ガリアファーム^{68}Ge／^{68}Gaジェネレータに関する資料

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Eckert & Ziegler Radiopharma GmbH

選任外国製造医薬品等製造販売業者

ノバルティスファーマ株式会社

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略号一覧

略号	省略していない表現 (英)	省略していない表現 (日)
^{68}Ga	Gallium-68	ガリウム 68
^{68}Ge	Germanium-68	ゲルマニウム 68
DOTA	1,4,7,10-Tetraazacyclododecane-tetraacetic acid	1,4,7,10-テトラアザシクロドデカン-四酢酸
DOTA-NOC	DOTA-Phe^1-Nal^3-octreotide	1,4,7,10-テトラアザシクロドデカン-1,4,7,10-四酢酸-フェニルアラニン-1-ヨウ化ナトリウム-3-オクトレオチド
DOTA-TATE	DOTA-D-Phe^1-Tyr^3-Thr^8-octreotate	1,4,7,10-テトラアザシクロドデカン-1,4,7,10-四酢酸-フェニルアラニン-1-チロシン-3-トレオニン-8-オクトレオチド
DOTA-TOC	DOTA-D-Phe^1-Tyr^3-octreotide	1,4,7,10-テトラアザシクロドデカン-1,4,7,10-四酢酸-フェニルアラニン-1-チロシン-3 オクトレオチド
EDTA	ethylenediaminetetraacetic acid	エチレンジアミン四酢酸
NET	neuroendocrine tumors	神経内分泌腫瘍
PET	positron emission tomography	陽電子放出断層撮影
PSMA	prostate-specific membrane antigen	前立腺特異的膜抗原

1 起原又は発見の経緯

ガリウム（^{68}Ga）は診断薬として1960年代初頭から利用可能となり最初に報告された臨床適用は^{68}Ga-エチレンジアミン四酢酸（以下，EDTA）で主な使用目的は脳病変の局在化であった。その後，標識抗体やアルブミンのような診断イメージングに有用な錯体の開発が進められ，特に有望であったのはソマトスタチン受容体陽性腫瘍の画像検査を目的とした^{68}Ga-DOTA標識ソマトスタチンアナログの開発，及び再発前立腺癌の画像検査を目的とした^{68}Ga標識PSMAの開発であった[2.5-1.3項]。^{68}Ga-DOTA標識ソマトスタチンアナログとして，2001年に^{68}Ga-DOTA-TOC，2005年に^{68}Ga-DOTA-NOC，2006年に^{68}Ga-DOTA-TATEが使用された。^{68}Ga-DOTA標識ペプチドは，少なくとも10年以上前から，神経内分泌腫瘍（NET）や髄膜腫の画像診断に使用されている[2.4-1.2項]。前立腺癌の画像診断に使用される診断薬の一つとして，[^{68}Ga]Ga-PSMA-11（以下，^{68}Ga-PSMA-11）と呼ばれる^{68}Ga-PSMAリガンド複合体がある。

ガリアファーム^{68}Ge/^{68}Gaジェネレータ｛[Germanium (^{68}Ge) chloride, Gallium (^{68}Ga) chloride] Radionuclide generator，治験成分記号EZR001，以下，本剤｝は，有効成分ガリウム（^{68}Ga）を含む塩化ガリウム（^{68}Ga）溶液を溶出するジェネレータ剤であり，患者に直接投与されることはない。^{68}Gaを標的部位に送達するためには，被標識用製剤に^{68}Gaを結合させる必要がある[2.5-1.1項，2.5-1.2項]。Eckert & Ziegler Radiopharma GmbH社が開発した本剤は，分散審査方式で欧州各国において承認され，2024年8月に中央審査方式でもEMAに承認された。本邦において，ノバルティスファーマ株式会社はEckert & Ziegler Radiopharma GmbH社の日本における選任外国製造医薬品等製造販売業者となるべく，本剤の医薬品製造販売承認申請（以下，承認申請）を行う。

2 本剤の治療上の位置付け

本剤は，有効成分ガリウム（^{68}Ga）を含む塩化ガリウム（^{68}Ga）溶液を溶出するジェネレータ剤であり，直接的な臨床適用はない[2.5-1.1項] 。^{68}Ga標識分子は主に，さまざまな腫瘍の陽電子放出断層撮影（PET）診断イメージングに用いられる。^{68}Ga，^{68}Ga-DOTA-TOC，^{68}Ga-DOTA-TATE，及び^{68}Ga-DOTA-NOCで放射標識したソマトスタチンアナログペプチドは最も重要な放射性医薬品であり，現在，多くのNET及び髄膜腫で過剰発現するさまざまなソマトスタチン受容体サブタイプの病変の画像検査及び鑑別に使用されている[2.5-1.2項]。

今回，前立腺特異的膜抗原（以下，PSMA）を標的とした治療薬 [^{177}Lu]Lu-PSMA-617（以下，AAA617） 及び診断薬PSMA-11と本剤は同時に承認申請を行う。本剤は，患者に直接投与されることはなく，PET診断のために，*in vitro* でPSMA-11を含めた被標識用製剤へのガリウム（^{68}Ga）標識に使用される予定である。

PSMA-11を被標識用製剤として使用する場合，本剤から溶出される塩化ガリウム（^{68}Ga）溶液をPSMA-11と混合し，キレート化した ^{68}Ga-PSMA-11を放射性診断薬として患者に静脈内投与し，PET検査を実施する。その際，本剤の1溶出あたり，PSMA-11の1バイアルが使用され，患者に投与される。PET検査の結果，PSMA陽性が確認された前立腺癌患者にPSMA標的療法を使

用する。したがって，本剤は PSMA-11 のガリウム（^{68}Ga）標識に必須であり，既存の代替薬は存在せず，PSMA 標的療法である AAA617 を投与するための患者選択に不可欠である。

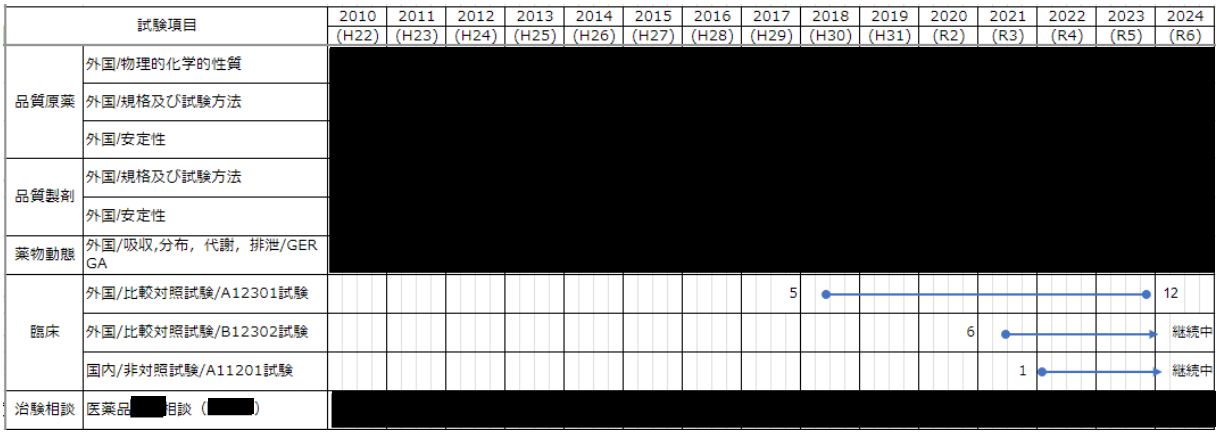
本邦では前立腺癌における PSMA 陽性病変を検出可能な画像診断は承認されておらず，本剤を用いたガリウム（^{68}Ga）標識後の ^{68}Ga-PSMA-11 PET 検査は国内初となる。また，研究用で使用されてきたサイクロトロンを用いたガリウム（^{68}Ga）製造と異なり，本剤及び PSMA-11 はそれぞれ医薬品として各施設に納入され，各施設で ^{68}Ga-PSMA-11 として調製された後，使用される。

3 開発の経緯

本項に関連する情報は，「2.5 臨床に関する概括評価 1 製品開発の根拠」にも記載した。

開発の経緯図を Figure 3-1 に示す。

Figure 3-1 開発の経緯図



3.1 品質に関する開発の経緯

本剤はジェネレータ剤で，ゲルマニウム（^{68}Ge）を塩化ゲルマニウム（^{68}Ge）の形でカラム充てんした二酸化チタンに吸着させ，これに塩化ガリウム（^{68}Ga）溶液を溶出させるために必要な装置及び不必要な被ばくを避けるために十分な遮へい装置を合わせたものである [2.3.P-2 項]。構成品として溶出用 0.1 mol/L 塩酸溶液及び溶出用チューブ等の各付属品があるが，溶出用 0.1 mol/L 塩酸溶液のみ個別で追加購入可能とする予定である。

本剤の承認申請にあたり，20[redacted] 年[redacted] 月に医薬品[redacted]相談（相談番号：[redacted]）を行い，[redacted]及び[redacted]について確認した。その結果，[redacted]，及び，[redacted]

[redacted]との見解を得た。また，[redacted]との見解を得た。加えて，[redacted]との見解を得た。

3.2 非臨床に関する開発の経緯

当該内容については，「2.4 非臨床試験の概括評価」に記載した。

3.3 臨床に関する開発の経緯

本剤より溶出した塩化ガリウム（^{68}Ga）溶液は直接患者に投与されず，被標識用製剤に ^{68}Ga を結合させるために用いられる。本剤の薬理作用，有効性，及び安全性は，標識に使用される塩化ガリウム（^{68}Ga）ではなく，最終的な標識医薬品の臨床特性のみによって決定されることから，^{68}Ga-PSMA-11 としての臨床的有用性を説明する必要があった。よって，本剤の承認申請においては，^{68}Ga-PSMA-11 を用いた検査により診断された PSMA 陽性の mCRPC 患者において AAA617 が投与された外国第 III 相試験である VISION 試験及び PSMAfore 試験，及び国内第 II 相試験である A11201 試験の結果で，臨床的有用性を説明することとした。

VISION 試験及び A11201 試験（パート 1/2）の結果から，1 種類以上の新規アンドロゲン受容体シグナル阻害薬（ARSI）の投与を受け，1 又は 2 種類のタキサンを含むレジメンによる治療歴がある PSMA 陽性の mCRPC 患者に対する AAA617 の有効性が確認された。また，PSMAfore 試験及び A11201 試験（パート 3）の結果から，1 種類の ARSI の治療歴があり，タキサンを含むレジメンを延期することが適切と考えられた PSMA 陽性の mCRPC 患者に対する AAA617 の有効性が確認された。これらの結果から，^{68}Ga-PSMA-11 の臨床的有用性が確認された。

以上より，PSMA-11 の承認申請と同時に ^{68}Ga-PSMA-11 の調製に使用する本剤，PSMA 標的療法である AAA617 をそれぞれ医薬品として承認申請を行うことが可能であると判断した。 本剤については，臨床データパッケージに基づき，「陽電子放出断層撮影（PET）イメージングのために承認された被標識用製剤のガリウム（^{68}Ga）標識」を効能又は効果（案）とした医薬品製造販売承認申請を行うこととした。

臨床データパッケージを「2.5 臨床に関する概括評価」に示す。

4 特徴及び有用性

本剤は，塩化ガリウム（^{68}Ga）溶液を溶出する製剤であり，様々な被標識用製剤をガリウム（^{68}Ga）標識可能である。

本剤は，付属又は追加購入可能な塩酸溶液を用いて，有効成分ガリウム（^{68}Ga）を含む塩化ガリウム（^{68}Ga）溶液を溶出するジェネレータ剤である。被標識用製剤を ^{68}Ga 標識することで，放射性診断薬として患者に静脈内投与し，PET 検査を実施する。

実際に $^{68}Ge/^{68}Ga$ ジェネレータは，DOTA 結合ペプチド標識用の放射性医薬品前駆体を得るために 10 年以上使用されており，^{68}Ga 標識分子は主に，さまざまな腫瘍状態の PET 診断イメージングに用いられている。^{68}Ga，^{68}Ga-DOTA-TOC，^{68}Ga-DOTA-TATE，及び ^{68}Ga-DOTA-NOC で標識したソマトスタチンアナログは最も重要な放射性医薬品であり，現在，多くの NET 及び髄膜腫で過剰発現するさまざまなソマトスタチン受容体サブタイプの病変の画像検査及び鑑別に使用されている。DOTA-TOC の ^{68}Ga 標識のためのキット製剤（SomaKit TOC®，Advanced Accelerator Applications 社）が EU で 2016 年 12 月に承認され，米国，カナダ，及びスイス等で同様のキットが製造販売承認を取得している[2.5-1.2 項]。また，DOTA-TATE（NETSPOT）は米国で承認取得しており，現在国内でも神経内分泌腫瘍患者を対象に第 III 相試験を実施中で，今後承認申請を予定している。

本剤を用いたガリウム（^{68}Ga）標識は，サイクロトロンと比較し簡易的であり，より多く施設で実施できる。

サイクロトロンを用いたガリウム（^{68}Ga）製造が実施されてきたが，サイクロトロンは大型機器であるため，導入できる施設は限られている。また，サイクロトロンで製造した場合，製造後にガリウム（^{68}Ga）のみに精製するプロセスも必要となる。本剤は放射性医薬品として医療機関に納入され，調剤する安全キャビネット内等に設置できる小型の製剤であり，サイクロトロンと比べ，より多くの施設で設置及び利用でき，必要なタイミングに必要量のガリウム（^{68}Ga）標識を簡易的に実施できる。本剤を用い，サイクロトロンを有しない医療機関でガリウム（^{68}Ga）標識が行えるようになることで，PET 検査のアクセス，利便性及び効率化の向上が期待される。

本剤を用いたガリウム（^{68}Ga）標識後の ^{68}Ga-PSMA-11 PET 検査は国内初の前立腺癌における PSMA 陽性病変を検出可能な PET 検査である。

PSMA は腺癌を含むほぼすべての前立腺癌に発現しているが，十二指腸粘膜，腎近位尿細管及び唾液腺等の一部の正常組織における発現は前立腺癌と比べ数百分の 1 と限定的である。また，PSMA の過剰発現は進行性，高悪性度，転移性，去勢抵抗性前立腺癌と相関することが示されている。さらに，PSMA 発現は予後不良の予測因子であり，PSMA の発現量が多い前立腺癌患者で

は生存期間が有意に短く再発リスクが高いことが報告されている。これらのことからも，PSMA を標的タンパク質として可視化することは，前立腺癌の新しい診断方法の一つとなり得る。

^{68}Ga-PSMA-11 の投与により PSMA 陽性が確認された mCRPC 患者を対象に PSMA 標的療法である AAA617 を投与した VISION 試験，PSMAfore 試験，及び A11201 試験のいずれの試験でも主要目的が達成され，AAA617 の有効性が認められた。また，^{68}Ga-PSMA-11 に臨床的に問題となる安全性上の懸念は認められなかった。したがって，PSMA 標的療法が有益と考えられる前立腺癌患者の選択に ^{68}Ga-PSMA-11 が利用可能であることが示された。

本邦では，前立腺癌における PSMA 陽性病変を検出可能な画像診断は承認されておらず，本剤を用いたガリウム（^{68}Ga）標識後の ^{68}Ga-PSMA-11 PET 検査は国内初となる。本剤は PSMA-11 のガリウム（^{68}Ga）標識に必須であり，さらに PSMA 標的療法である AAA617 を投与するための患者選択にも不可欠である。

5 まとめ

以上を踏まえ，以下のとおり本剤の製造販売承認申請を行う。

【申請品目】

ガリアファーム ^{68}Ge/^{68}Ga ジェネレータ

【効能又は効果（案）】

陽電子放出断層撮影（PET）イメージングのために承認された被標識用製剤のガリウム（^{68}Ga）標識

【用法及び用量（案）】

標識に必要な塩化ガリウム（^{68}Ga）溶液の量及びその後投与する ^{68}Ga 標識医薬品の量は、標識する医薬品とその使用目的によって異なる。標識する個別の医薬品の電子添文を参照すること。

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表 一 覧

Table 1-1　主要国での承認状況 3

1 外国における使用状況等

本剤は 2014 年 9 月にイタリアで最初の製造販売承認を取得し，2025 年 6 月現在，米国及びオーストラリアを除き，欧州，英国，カナダ等 8 つの国又は地域で承認されている。主要国での承認状況を，Table1-1 に示す。

Table 1-1 主要国での承認状況

国名	承認年月日	効能・効果
欧州	2024 年 8 月 1 日	ガリウムジェネレータからの溶出液（塩化ガリウム（^{68}Ga）溶液）を用いた，陽電子放出断層撮影（PET）イメージングのために開発・承認された放射性医薬品調製用キットの *in vitro* 放射線標識
英国	2017 年 8 月 1 日	ガリウムジェネレータからの溶出液（塩化ガリウム（^{68}Ga）溶液）を用いた，陽電子放出断層撮影（PET）イメージングのために開発・承認された放射性医薬品調製用キットの *in vitro* 放射線標識
カナダ	2020 年 8 月 19 日	陽電子放出断層撮影（PET）での診断イメージングに使用する放射性医薬品を調製するための標識用に開発及び承認された担体分子の *in vitro* 放射線標識

2 外国の添付文書等の概要

Eckert & Ziegler Radiopharma GmbH 社にて企業中核データシート（CCDS）は作成されていない。最新の EU 共通の添付文書を提出する。

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

GalliaPharm 1.11 GBq radionuclide generator
GalliaPharm 1.48 GBq radionuclide generator
GalliaPharm 1.85 GBq radionuclide generator
GalliaPharm 2.22 GBq radionuclide generator
GalliaPharm 2.59 GBq radionuclide generator
GalliaPharm 2.96 GBq radionuclide generator
GalliaPharm 3.33 GBq radionuclide generator
GalliaPharm 3.70 GBq radionuclide generator

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The radionuclide generator contains germanium (^{68}Ge) as mother nuclide which decays to the daughter nuclide gallium (^{68}Ga). The germanium (^{68}Ge) used for the production of the (^{68}Ge/^{68}Ga) generator is no carrier added. The total radioactivity due to germanium (^{68}Ge) and gamma-ray-emitting impurities in the eluate is not more than 0.001 %.

The GalliaPharm 1.11 - 3.70 GBq radionuclide generator is a system for the elution of sterile gallium (^{68}Ga) chloride solution for radiolabelling in accordance with Ph. Eur. 2464. This solution is eluted from a column on which the mother nuclide germanium (^{68}Ge), parent of gallium (^{68}Ga), is fixed. The system is shielded. Physical characteristics of both mother and daughter nuclides are summarised in table 1.

Table 1: Physical characteristics of germanium (^{68}Ge) and gallium (^{68}Ga)

	^{68}Ge	**^{68}Ga**
Half-life	270.95 days	67.71 minutes
Type of physical decay	Electron capture	Positron emission
X-rays	9.225 keV (13.1 %) 9.252 keV (25.7 %) 10.26 keV (1.64 %) 10.264 keV (3.2 %) 10.366 keV (0.03 %)	8.616 keV (1.37 %) 8.639 keV (2.69 %) 9.57 keV (0.55 %)
Gamma-rays		511 keV (178.28 %) 578.55 keV (0.03 %) 805.83 keV (0.09 %) 1,077.34 keV (3.22 %) 1,260.97 keV (0.09 %) 1,883.16 keV (0.14 %)
Beta+		Energy max. Energy 352.60 keV 821.71 keV (1.20 %) 836.00 keV 1,899.01 keV (87.94 %)

Data derived from nudat (www.nndc.bnl.gov)

5 ml of the eluate from the radionuclide generator with highest strength (3.70 GBq) contains a potential maximum of 3.70 GBq of ^{68}Ga and 0.000037 GBq (37 kBq) of ^{68}Ge (0.001 % breakthrough in the eluate). This corresponds to 2.4 ng of gallium and 0.14 ng of germanium.

The quantity of gallium (^{68}Ga) chloride solution for radiolabelling Ph.Eur. that may be eluted from the radionuclide generator is dependent on the quantity of germanium (^{68}Ge) present on the date/time of elution, the volume of eluent used (typically 5 ml), and the lapsed time since the previous elution. If mother and daughter nuclides are in equilibrium, more than 60 % of the present gallium (^{68}Ga) activity can be eluted.

Table 2 summarises the activity on the radionuclide generator, the minimum activities obtained by elution at the start of the shelf-life and at the end of the shelf-life as well as the potential maxima of ^{68}Ga and ^{68}Ge in the eluate.

Table 2: Activity on the radionuclide generator and activity obtained by elution

Strength, GBq	**Activity inside the radionuclide generator at the start of shelf-life*, GBq**	**Activity inside the radionuclide generator at the end of shelf-life*, GBq**	**Eluted activity at the start of shelf-life**, GBq**	**Potential maximum amount of ^{68}Ga in 5 ml eluate, GBq / ng**	**Potential maximum amount of ^{68}Ge in 5 ml eluate, kBq / ng**	**Eluted activity at the end of shelf-life**, GBq**
1.11	1.11	0.27	NLT 0.67	1.11 / 0.73	11.1 / 0.04	NLT 0.16
1.48	1.48	0.36	NLT 0.89	1.48 / 0.98	14.8 / 0.06	NLT 0.22
1.85	1.85	0.46	NLT 1.11	1.85 / 1.22	18.5 / 0.07	NLT 0.27
2.22	2.22	0.55	NLT 1.33	2.22 / 1.47	22.2 / 0.08	NLT 0.33
2.59	2.59	0.64	NLT 1.55	2.59 / 1.71	25.9 / 0.10	NLT 0.38
2.96	2.96	0.73	NLT 1.78	2.96 / 1.96	29.6 / 0.11	NLT 0.44
3.33	3.33	0.82	NLT 2.00	3.33 / 2.20	33.3 / 0.13	NLT 0.49
3.70	3.70	0.91	NLT 2.22	3.70 / 2.45	37.0 / 0.14	NLT 0.55

NLT = not less than
** The actual activity inside the radionuclide generator may deviate by ± 10 % from the nominal strength*
*** In equilibrium*

More detailed explanations and examples for elutable activities at various time points are given in section 12.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Radionuclide generator.

The radionuclide generator is presented as an unstained stainless-steel case with two handles and an inlet and an outlet port.

The radionuclide generator provides after elution a sterile gallium (^{68}Ga) chloride solution for radiolabelling. The solution is clear and colourless.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This radionuclide generator is not intended for direct use in patients.

The sterile eluate (gallium (^{68}Ga) chloride solution) from the radionuclide generator GalliaPharm is indicated for *in vitro* radiolabelling of various kits for radiopharmaceutical preparation developed and approved for radiolabelling with such eluate, to be used for positron emission tomography (PET) imaging.

4.2 Posology and method of administration

This medicinal product is for use in designated nuclear medicine facilities only and should only be handled by specialists experienced with *in vitro* radiolabelling.

Posology

The quantity of the eluate gallium (^{68}Ga) chloride solution required for radiolabelling and the quantity of ^{68}Ga-labelled radiopharmaceutical that is subsequently administered will depend on the kit that is to be radiolabelled and its intended use. Refer to the Summary of Product Characteristics/package leaflet of the particular kit for radiopharmaceutical preparation to be radiolabelled.

Paediatric population

Please refer to the Summary of Product Characteristics/package leaflet of the kit for radiopharmaceutical preparation to be radiolabelled with ^{68}Ga for more information concerning its paediatric use.

Method of administration

The gallium (^{68}Ga) chloride solution is not intended for direct use in patients but is used for *in vitro* radiolabelling of various kits for radiopharmaceutical preparation. The route of administration of the ^{68}Ga-labelled radiopharmaceutical is defined in the Summary of Product Characteristics/package leaflet of the respective kit for radiopharmaceutical preparation and should be adhered to.

For instructions on extemporary preparation of the medicinal product before administration, see section 12.

4.3 Contraindications

Gallium (^{68}Ga) chloride solution should not be administered directly to the patient.

The use of ^{68}Ga-labelled medicinal products is contraindicated in case of hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

For information on contraindications to particular ^{68}Ga-labelled radiopharmaceuticals prepared by radiolabelling with gallium (^{68}Ga) chloride solution, refer to the Summary of Product Characteristics/package leaflet of the particular medicinal product to be radiolabelled.

4.4 Special warnings and precautions for use

Gallium (^{68}Ga) chloride solution for radiolabelling is not to be administered directly to the patient but is used for *in vitro* radiolabelling of various kits for radiopharmaceutical preparation.

Unintended direct administration of gallium (^{68}Ga) chloride solution may lead to increased radiation exposure to patients (see sections 4.9, 5.2, and 11). Accidental administration of gallium (^{68}Ga)

chloride solution for radiolabelling containing 0.1 mol/l hydrochloric acid may also cause local venous irritation and, in case of paravenous injection, tissue necrosis. The catheter or affected area should be irrigated with 9 mg/ml (0.9 %) sodium chloride solution for injection.

Safe handling of GalliaPharm and its eluate in accordance with the instructions in this document should be permanently ensured to protect patients and healthcare professionals from unintentional excess radiation exposure (see sections 6 and 12).

^{68}Ge breakthrough can increase in the eluate above 0.001 % if the radionuclide generator is not eluted for several days (see section 12). All instructions provided in section 12 should be strictly followed to avoid the risk of excess exposure to ^{68}Ge.

Individual benefit/risk justification

For each patient, the radiation exposure must be justifiable by the likely benefit.
The radioactivity administered should in every case be as low as reasonably achievable to obtain the required information.

General warnings

For information concerning special warnings and special precautions for use of ^{68}Ga-labelled radiopharmaceuticals refer to the Summary of Product Characteristics/package leaflet of the kit for radiopharmaceutical preparation to be radiolabelled.

Precautions with respect to environmental hazard are included in section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies of the gallium (^{68}Ga) chloride solution for radiolabelling with other medicinal products have been performed, because it is used for *in vitro* radiolabelling of medicinal products.

For information concerning interactions associated with the use of ^{68}Ga-labelled radiopharmaceuticals, refer to the Summary of Product Characteristics/package leaflet of the kit for radiopharmaceutical preparation to be radiolabelled.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy

Radionuclide procedures carried out on pregnant women also involve radiation dose to the foetus. Only essential investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and the foetus.

Breast-feeding

Before administering a radiopharmaceutical to a mother who is breast-feeding, consideration should be given to whether the investigation could be reasonably delayed until the mother has ceased breast-feeding. If the administration is considered necessary, breast-feeding should be interrupted, and the expressed feeds discarded.

Further information concerning the use of a ^{68}Ga-labelled radiopharmaceutical in pregnancy and breast-feeding is specified in the Summary of Product Characteristics/package leaflet of the kit for radiopharmaceutical preparation to be radiolabelled.

Fertility

Further information concerning the use of a ^{68}Ga-labelled radiopharmaceutical concerning fertility is specified in the Summary of Product Characteristics/package leaflet of the kit for radiopharmaceutical preparation to be radiolabelled.

4.7 Effects on ability to drive and use machines

Effects on ability to drive and use machines following administration of ^{68}Ga-labelled radiopharmaceutical will be specified in the Summary of Product Characteristics/package leaflet of the kit for radiopharmaceutical preparation to be radiolabelled.

4.8 Undesirable effects

Possible adverse reactions following the use of a ^{68}Ga-labelled radiopharmaceutical will be dependent on the specific kit for radiopharmaceutical preparation being used. Such information will be supplied in the Summary of Product Characteristics/package leaflet of the kit for radiopharmaceutical preparation to be radiolabelled.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Excess radiation exposure may occur if higher than recommended activity of a ^{68}Ga-labelled radiopharmaceutical is administered to a patient. For further information refer to the Summary of Product Characteristics/package leaflet of the kit for radiopharmaceutical preparation to be radiolabelled.

No toxic effects are to be expected from the free ^{68}Ga after an inadvertent administration of the eluate. The administered free ^{68}Ga decays almost completely to stable ^{68}Zn within a short time (97 % are decayed in 6 hours). During this time, ^{68}Ga is mainly concentrated in the blood/plasma (bound to transferrin) and in the urine. The patient should be hydrated to increase the excretion of the ^{68}Ga. Forced diuresis as well as frequent bladder voiding are recommended.

Human radiation dose in case of an inadvertent administration of the eluate should be estimated using the information given in section 11.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceuticals; other diagnostic radiopharmaceuticals, ATC code: V09X.

The pharmacodynamic properties of ^{68}Ga-labelled radiopharmaceutical prepared by radiolabelling with the radionuclide generator eluate prior to administration will be dependent on the nature of the carrier molecule to be labelled. Refer to the Summary of Product Characteristics/package leaflet of the kit for radiopharmaceutical preparation to be radiolabelled.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with GalliaPharm 1.11 – 3.70 GBq radionuclide generator in all subsets of the paediatric population as it is a radiolabelling agent. See section 4.2 for information on paediatric use.

5.2 Pharmacokinetic properties

Gallium (^{68}Ga) chloride solution is not intended for direct use in patients but is used for *in vitro* radiolabelling of various kits for radiopharmaceutical preparation. Therefore, the pharmacokinetic properties of ^{68}Ga-labelled radiopharmaceuticals will depend on the nature of carrier molecules to be radiolabelled.

The absorption, distribution, and excretion of free ^{68}Ga following direct injection of gallium (^{68}Ga) chloride solution were investigated in rats. The rat study has shown that following direct intravenous administration of gallium (^{68}Ga) chloride, ^{68}Ga is slowly cleared from the blood with a biological half-life of 188 h in male and 254 h in female rats. This is because free Ga^{3+} likely behaves in a similar way as Fe^{3+}. However, as the biological half-life of ^{68}Ga is much longer than its physical half-life (67.71 min), at 188 h or 254 h almost all ^{68}Ga anyway decays to inactive ^{68}Zn. Already in 6 h approx. 97 % of the initial ^{68}Ga disappear via decay to ^{68}Zn.

In rats, ^{68}Ga was excreted predominantly into the urine, with some retention in the liver and kidneys. The organs with the highest ^{68}Ga activity, other than blood, plasma, and urine, were liver, lungs, spleen, and bones. In female rats, the ^{68}Ga activity in female genital organs, i.e., uterus and ovaries, was comparable to that seen in the lungs. ^{68}Ga activity in the testes was very low.

Extrapolating from the rat data, the estimated sex-averaged effective dose resulting from an inadvertently intravenously injected gallium (^{68}Ga) chloride would be 0.0216 mSv/MBq for an adult (see section 11 for more details).

The activity resulting from ^{68}Ge breakthrough in the rat study was extremely low and is not of clinical importance.

5.3 Preclinical safety data

The toxicological properties of ^{68}Ga-labelled radiopharmaceuticals prepared by *in vitro* radiolabelling with gallium (^{68}Ga) chloride solution will depend on the nature of the kit for radiopharmaceutical preparation to be radiolabelled.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Column matrix

Titanium dioxide

Solution for elution

Sterile ultrapure 0.1 mol/l hydrochloric acid

6.2 Incompatibilities

Radiolabelling of carrier molecules with gallium (^{68}Ga) chloride is very sensitive to the presence of trace metal impurities.

It is important that all glassware, syringe needles etc., used for the preparation of the radiolabelled medicinal product are thoroughly cleaned to ensure freedom from such trace metal impurities. Only syringe needles (for example, non-metallic) with proven resistance to dilute acids should be used to minimise trace metal impurity levels.

It is recommended not to use uncoated stoppers for the elution vial as they may contain considerable amounts of zinc that is extracted by the acidic eluate.

6.3 Shelf life

Radionuclide generator

18 months from calibration date.
The calibration date and the expiry date are stated on the label.

Gallium (^{68}Ga) chloride solution for radiolabelling

After elution, immediately use the eluate.

Sterile ultrapure hydrochloric acid solution for elution

2 years.

6.4 Special precautions for storage

Warm temperatures substantially exceeding 25 °C can reversibly reduce the yield of ^{68}Ga in the eluate to below 60 %. Therefore, to obtain optimal elution yield (> 60 %), the radionuclide generator should be operated at temperatures not exceeding 25 °C. If the radionuclide generator is routinely stored at higher temperatures, make sure to equilibrate it at < 25 °C for several hours before elution. Elutions at temperatures above 25 °C are nevertheless possible and will not harm the radionuclide generator or have an impact on the quality of the eluate except for the possibly reduced yield of ^{68}Ga.

Storage of radiopharmaceuticals should be in accordance with national regulations on radioactive materials.

6.5 Nature and contents of container and special equipment for use

The glass column consists of a borosilicate glass tube (type I) and Polyetheretherketone (PEEK) end plugs which are attached to PEEK inlet and outlet lines via HPLC-style fingertight fittings. These lines are connected to two ports that pass through the outer case of the radionuclide generator.

The column is contained within the lead shield assembly. The shield assembly is secured in a stainless-steel outer case with two handles.

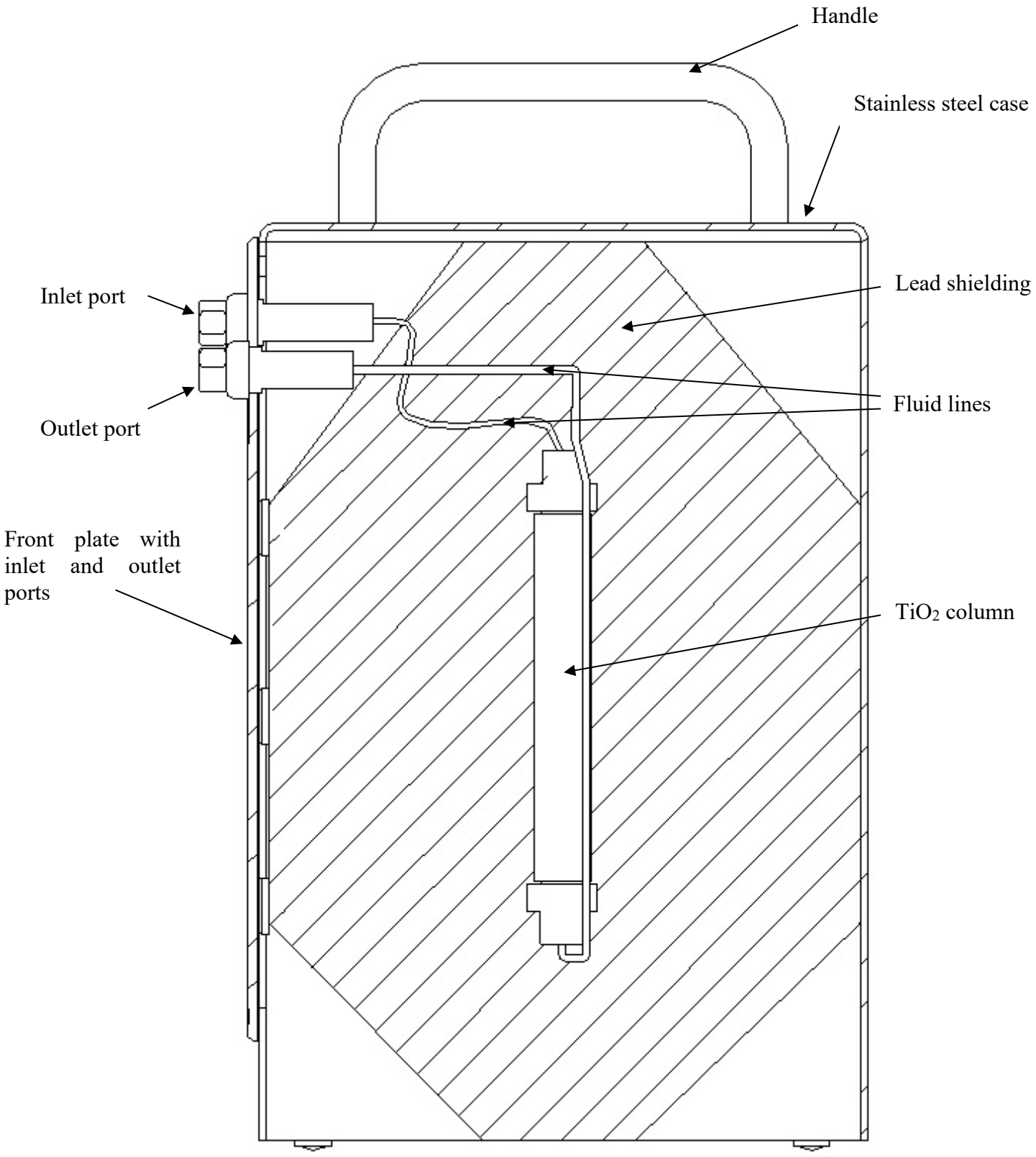
Accessories supplied with the radionuclide generator (minimum amounts):

1. 1 x PP – container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid (including a separate hanger for PP-bottles; PP = Polypropylene)
2. 1 x Vented spike (ABS = Acrylonitrile Butadiene Styrene/PE = Polyethylene)
3. 2 x Adapter 1/16" to male LUER (PEEK)
4. 2 x Tubing 60 cm (PEEK)
5. 1 x Tubing 40 cm (PEEK)
6. 1 x Tubing 20 cm (PEEK)
7. 3 x Fingertight fitting 1/16" 10-32 (PEEK)
8. 1 x Fingertight fitting 1/16" M6 (PEEK)
9. 1 x Stopcock manifold (TPX = Polymethylpentene/HDPE = High Density Polyethylene)
10. 1 x Male LUER union (PP)

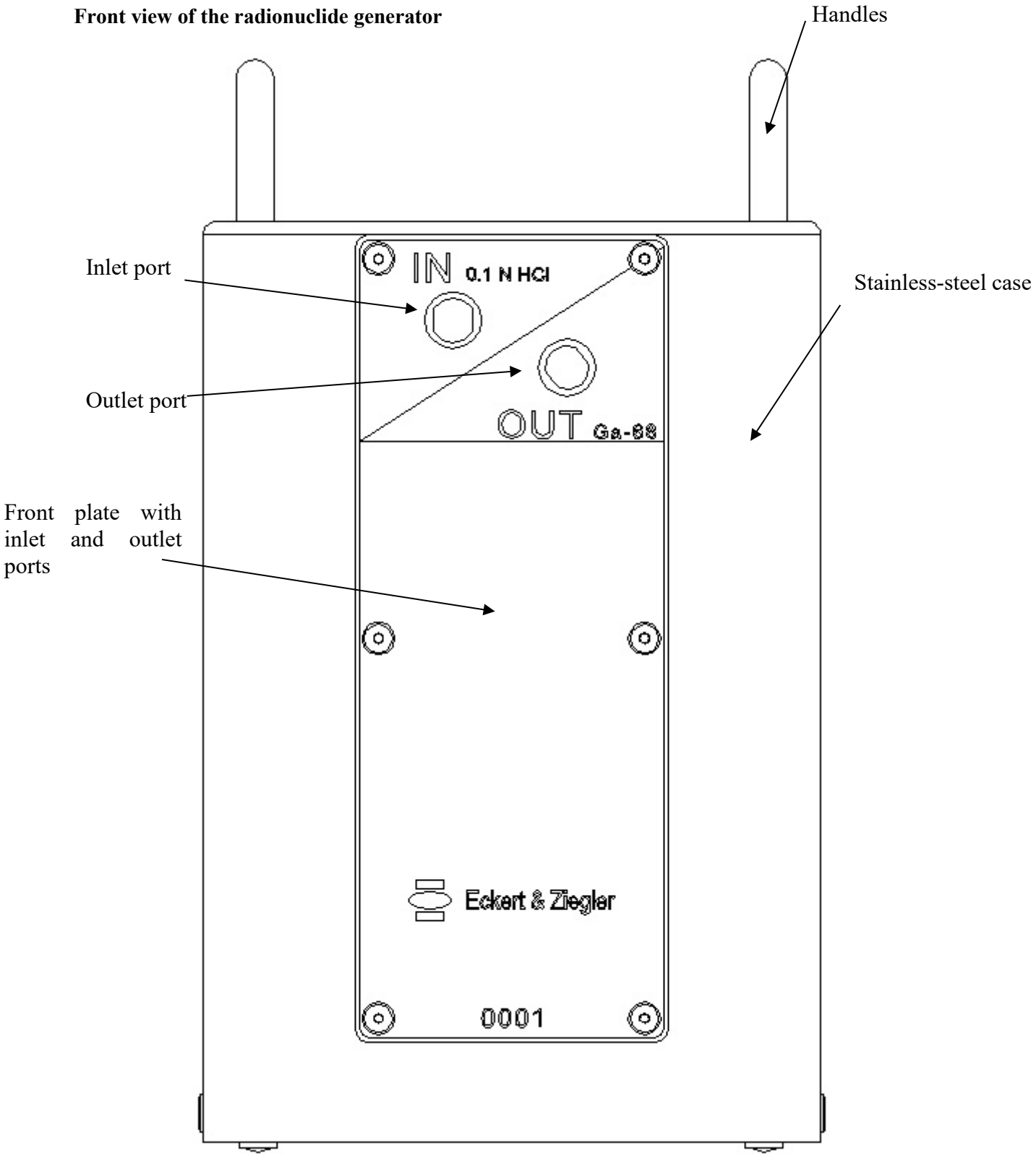
Pack sizes:

The radionuclide generators are supplied with the following ^{68}Ge activity amounts at calibration date: 1.11 GBq, 1.48 GBq, 1.85 GBq, 2.22 GBq, 2.59 GBq, 2.96 GBq, 3.33 GBq, and 3.70 GBq.

Sectional view of the radionuclide generator



Front view of the radionuclide generator



Size: 230 mm x 132 mm x 133 mm (H x W x D)

Weight: approx. 14 kg

6.6 Special precautions for disposal and other handling

General warnings

Radiopharmaceuticals should be received, used, and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of the competent official organisation.

Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

The radionuclide generator must not be disassembled for any reason as this may damage the internal components and possibly lead to a leak of radioactive material. Also, disassembly of the stainless-steel case will expose the lead shielding to the operator.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

The residual activity of the radionuclide generator must be estimated before disposal.

Any unused gallium (^{68}Ga) chloride solution for radiolabelling or radiolabelled medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1836/001 - GalliaPharm 1.11 GBq radionuclide generator
EU/1/24/1836/002 - GalliaPharm 1.48 GBq radionuclide generator
EU/1/24/1836/003 - GalliaPharm 1.85 GBq radionuclide generator
EU/1/24/1836/004 - GalliaPharm 2.22 GBq radionuclide generator
EU/1/24/1836/005 - GalliaPharm 2.59 GBq radionuclide generator
EU/1/24/1836/006 - GalliaPharm 2.96 GBq radionuclide generator
EU/1/24/1836/007 - GalliaPharm 3.33 GBq radionuclide generator
EU/1/24/1836/008 - GalliaPharm 3.70 GBq radionuclide generator

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

11. DOSIMETRY

The radiation dose received by the various organs following intravenous administration of a ^{68}Ga-radiolabelled medicinal product is dependent on the specific kit for radiopharmaceutical preparation being radiolabelled. Information on radiation dosimetry of each different ^{68}Ga-labelled radiopharmaceutical following its administration will be available in the Summary of Product Characteristics of the particular kit for radiopharmaceutical preparation.

The dosimetry tables 3 and 4 below are presented in order to support the assessment of the contribution by unbound ^{68}Ga to the radiation dose following the administration of ^{68}Ga-labelled radiopharmaceutical or of the radiation dose resulting from an inadvertent intravenous injection of gallium (^{68}Ga) chloride solution.

The dosimetry estimates were based on a rat distribution study. Time points for measurements were 5 minutes, 30 minutes, 60 minutes, 120 minutes, and 180 minutes.

The effective radiation dose of ^{68}Ga for an adult is 0.0216 mSv/MBq, resulting in an approximate effective radiation dose of 5.6 mSv from an accidental intravenously injected activity of 259 MBq.

Table 3: Absorbed dose per unit activity administered - inadvertent administration of the eluate - gallium (^{68}Ga) chloride - in women

Absorbed dose per administered unit of activity (mGy/MBq)						
Organ	**Adult[1] (60 kg)**	**15 years[2] (50 kg)**	**10 years[2] (30 kg)**	**5 years[2] (17 kg)**	**1 year[2] (10 kg)**	**Newborn[2] (5 kg)**
Adipose/residual tissue	0.0121	0.0199	0.0327	0.0531	0.1050	0.2680
Adrenals	0.0398	0.0304	0.0440	0.0618	0.0959	0.1020
Bone marrow	0.0299	0.0202	0.0331	0.0606	0.1540	0.6050
Bone surface	0.0169	ND	ND	ND	ND	ND
Brain	0.0081	0.0048	0.0061	0.0081	0.0126	0.0282
Colon wall	0.0210	0.0224	0.0373	0.0609	0.1170	0.2930
Heart wall	0.0838	0.0263	0.0407	0.0639	0.1150	0.2280
Kidneys	0.0424	0.0333	0.0474	0.0712	0.1280	0.3250
Liver	0.0640	0.0598	0.0906	0.1360	0.2630	0.6080
Lungs	0.0552	0.0497	0.0708	0.1090	0.2160	0.5840
Muscle	0.0131	0.0131	0.0248	0.0698	0.1370	0.1950
Osteogenic cells	0.0567[2]	0.0558	0.0869	0.1420	0.3310	1.0100
Ovaries	0.0372	0.0332	0.0944	0.1650	0.3720	0.7550
Pancreas	0.0309	0.0276	0.0533	0.0704	0.1490	0.4730
Salivary glands	0.0194	ND	ND	ND	ND	ND
Skin	0.0115	0.0115	0.0189	0.0311	0.0612	0.1570
Small intestine wall	0.0256	0.0273	0.0459	0.0749	0.1460	0.3630
Spleen	0.0407	0.0263	0.0403	0.0642	0.1180	0.3030
Stomach wall	0.0284	0.0188	0.0293	0.0482	0.0939	0.2540
Thymus	0.0129	0.0094	0.0115	0.0157	0.0261	0.0518
Thyroid	0.0265	0.0282	0.0434	0.0923	0.1730	0.2490
Urinary bladder wall[4]	0.0174	0.0155	0.0251	0.0419	0.0770	0.2000
Uterus/cervix	0.0291	0.0325	0.4560	0.6900	1.2500	0.5360
Effective dose (mSv/MBq)	0.0216[3]					

ND = not determined as organ/tissue not available in OLINDA/EXM v1.0.

[1] calculations made in IDAC-Dose 2.1 v1.01 software.

[2] calculations made in OLINDA v1.0 software.

[3] sex-averaged dose derived according to ICRP Publication 103.

[4] Due to the methodological limitations of the underlying distribution study in rats, it was not feasible to consider urinary bladder content as an explicit source region for the dosimetry. Since gallium (^{68}Ga) chloride is excreted predominantly into the urine according to the rat data, the reported effective dose is thus possibly underestimated.

Table 4: Absorbed dose per unit activity administered – inadvertent administration of the eluate - gallium (^{68}Ga) chloride - in men

Absorbed dose per administered unit of activity (mGy/MBq)						
Organ	**Adult[1] (73 kg)**	**15 years[2] (50 kg)**	**10 years[2] (30 kg)**	**5 years[2] (17 kg)**	**1 year[2] (10 kg)**	**Newborn[2] (5 kg)**
Adipose/residual tissue	0.0065	0.0128	0.0210	0.0341	0.0672	0.1720
Adrenals	0.0189	0.0200	0.0289	0.0405	0.0628	0.0669
Bone marrow	0.0124	0.0149	0.0244	0.0454	0.1120	0.4180
Bone surface	0.0079	ND	ND	ND	ND	ND
Brain	0.0046	0.0034	0.0043	0.0056	0.0088	0.0196
Colon wall	0.0121	0.0162	0.0274	0.0449	0.0865	0.2150
Heart wall	0.0335	0.0195	0.0303	0.0478	0.0858	0.1710
Kidneys	0.0221	0.0239	0.0340	0.0510	0.0915	0.2340
Liver	0.0307	0.0388	0.0588	0.0881	0.1700	0.3940
Lungs	0.0262	0.0327	0.0466	0.0718	0.1420	0.3850
Muscle	0.0072	0.0111	0.0219	0.0658	0.1300	0.1800
Osteogenic cells	0.0308[2]	0.0402	0.0633	0.1050	0.2440	0.7550
Pancreas	0.0167	0.0211	0.0412	0.0540	0.1150	0.3720
Salivary glands	0.0132	ND	ND	ND	ND	ND
Skin	0.0073	0.0063	0.0102	0.0166	0.0326	0.0828
Small intestine wall	0.0126	0.0167	0.0282	0.0460	0.0892	0.2220
Spleen	0.0238	0.0259	0.0400	0.0634	0.1170	0.3060
Stomach wall	0.0145	0.0116	0.0179	0.0295	0.0573	0.1570
Testes	0.0098	0.0182	0.1210	0.1410	0.1910	0.2770
Thymus	0.0092	0.0082	0.0093	0.0122	0.0193	0.0384
Thyroid	0.0163	0.0248	0.0383	0.0825	0.1550	0.2200
Urinary bladder wall[4]	0.0116	0.0095	0.0151	0.0252	0.0458	0.1190
Small intestine wall	0.0126	0.0167	0.0282	0.0460	0.0892	0.2220
Effective dose (mSv/MBq)	0.0216[3]					

ND = not determined as organ/tissue not available in OLINDA/EXM v1.0.

[1] calculations made in IDAC-Dose 2.1 v1.01 software.

[2] calculations made in OLINDA v1.0 software.

[3] sex-averaged dose derived according to ICRP Publication 103.

[4] Due to the methodological limitations of the underlying distribution study in rats, it was not feasible to consider urinary bladder content as an explicit source region for the dosimetry. Since gallium (^{68}Ga) chloride is excreted predominantly into the urine according to the rat data, the reported effective dose is thus possibly underestimated.

External radiation exposure

The average surface or contact radiation for the radionuclide generator is less than 0.14 µSv/h per MBq of ^{68}Ge, but local hot spots of higher radiation can occur. Nevertheless, a 3.70 GBq radionuclide generator will reach an overall average surface dose rate of approx. 518 µSv/h. It is generally recommended that the radionuclide generator is stored within auxiliary shielding to minimise dose to operating personnel.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Elution of the radionuclide generator must be performed in premises complying with the national regulations concerning the safety of use of radioactive products.

The general handling, the attachment of tubing, the exchange of the sterile ultrapure 0.1 mol/l hydrochloric acid container, the elution of the generator and other activities potentially exposing the generator to the environment should be undertaken using aseptic techniques in an appropriate clean environment according to current national legislation.

Preparation

Unpacking of the radionuclide generator:

1. Check outer shipping package for shipping damage. If damaged, perform radiation wipe survey of the damaged area. If counts exceed 40 counts per second per 100 cm^2, notify your Radiation Safety Officer.

2. Cut security seal on top of shipping package. Remove the inner foam support from the shipping package. Separate the foam elements carefully.

3. Carefully remove radionuclide generator.

   CAUTION: Drop hazard: The radionuclide generator weighs approx. 14 kg. Handle with care to avoid potential injuries. If radionuclide generator is dropped or if shipping damage extends into the shipping package, check for leaks and perform a wipe survey of the radionuclide generator. Also check for internal damage by slowly tilting the radionuclide generator 90°. Listen for broken/loose parts.

4. Perform wipe survey of shipping package inserts and radionuclide generator outer surface. If wipes exceed 40 counts per second per 100 cm^2, notify your Radiation Safety Officer.

5. Check sealed inlet and outlet ports for damage. Do not remove the port plugs before the elution lines are prepared and ready for installation.

Optimal positioning:

1. When installing the radionuclide generator in its final position, i.e., with a synthesis device or for manual elutions, it is recommended to keep the outlet line as short as possible as the length of this tubing may influence the yield in the receiving/reaction vial. For this reason, the radionuclide generator is supplied with three different lengths of tubing to choose the appropriate length.

2. Local auxiliary shielding is recommended when positioning the radionuclide generator.

Please note: Moving the radionuclide generator after installation in its final position should be avoided.

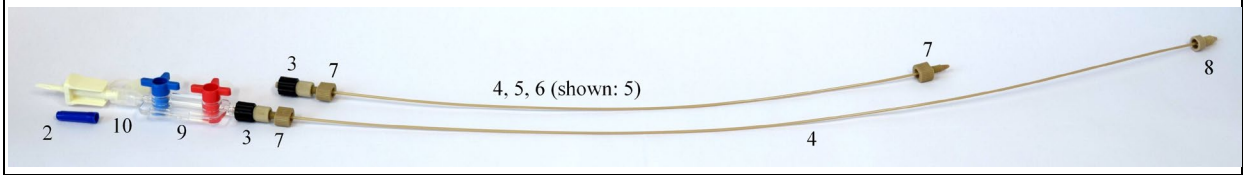
Assembly of the radionuclide generator:

Accessories supplied with the radionuclide generator (minimum amounts):

1. 1 x PP – container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid (including a separate hanger for PP-bottles; PP = Polypropylene)
2. 1 x Vented spike (ABS = Acrylonitrile Butadiene Styrene/PE = Polyethylene).
3. 2 x Adapter 1/16" to male LUER (PEEK)
4. 2 x Tubing 60 cm (PEEK)
5. 1 x Tubing 40 cm (PEEK)
6. 1 x Tubing 20 cm (PEEK)
7. 3 x Fingertight fitting 1/16" 10-32 (PEEK)
8. 1 x Fingertight fitting 1/16" M6 (PEEK)
9. 1 x Stopcock manifold (TPX = Polymethylpentene/HDPE = High Density Polyethylene)
10. 1 x Male LUER union (PP)

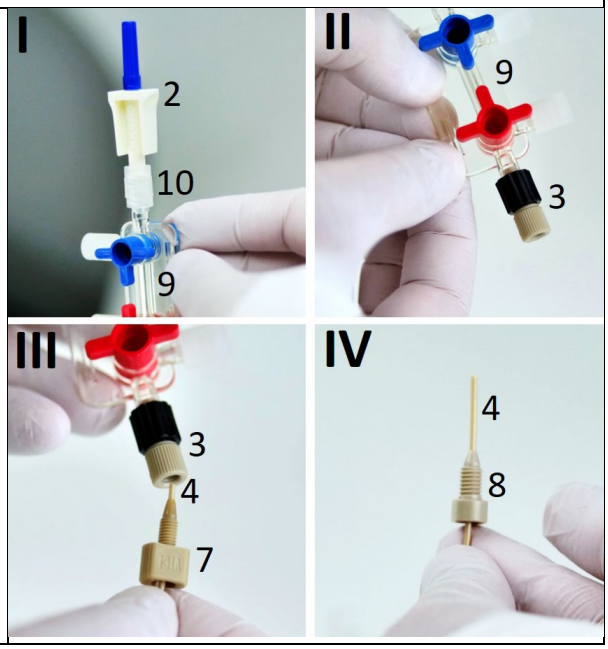
Assemble the radionuclide generator in an appropriately clean environment. Aseptic working technique must be maintained during the whole assembly process. Wear gloves during preparation and connecting of the lines to the radionuclide generator and to the eluent container. This is critical for the maintenance of sterility.

Picture of assembled elution accessories before connection to the radionuclide generator (The indicated identification numbers of accessories are as presented in the list above. They are also used accordingly in the pictures and assembly instructions following below.):



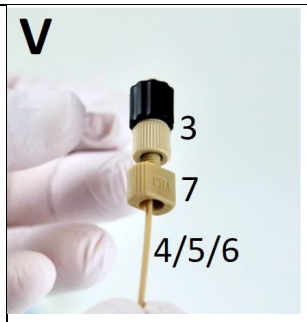
1. Assembling the inlet line:

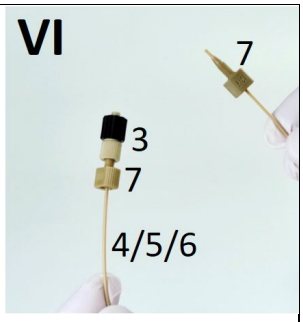
Please note: the inlet port has a customised thread to avoid misconnection. Only the special fingertight fitting 1/16" M6 will fit into this port. For assembling the inlet line, connect the vented spike (2) to one end of the stopcock manifold (9) using the male LUER union (10) **[I]**. On the other end of the stopcock manifold (9) connect the adapter 1/16" to male LUER (3) **[II]**. Attach one of the 60 cm long PEEK tubing (4) with a 1/16" 10-32 fingertight fitting (7) **[III]**. Put the special 1/16" M6 fingertight fitting (8) on the other end of the line, <u>but do not connect yet</u> **[IV]**.



2. Assembling the outlet line:

For the outlet line, choose the appropriate length of tubing (20 cm, 40 cm, or 60 cm) based on your local setting. Use the shortest line possible. Attach the chosen PEEK line (4,5 or 6) to the second adapter 1/16" to male LUER (3) using a 1/16" 10-32 fingertight fitting (7) **[V]**. Put the third 1/16" 10-32 fingertight fitting (7) on the other end of the prepared outlet line, but do not connect yet **[VI]**.





3. Connecting the hydrochloric acid container to the inlet line:

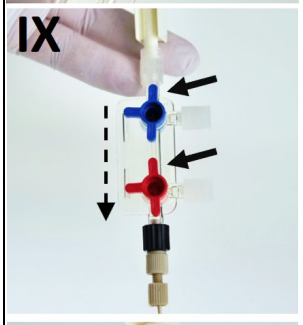
Hang the PP - container with the 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid solution close to the inlet port above the radionuclide generator.
The valves of the stopcock manifold have a T-type flow pattern with three openings inside - one in each direction of the external prongs. Turn the valves at the stopcock manifold in the appropriate direction (3-6-9 clock position ⊤) so that no liquid can enter through the spike **[VII].** Remove the lid of the vented spike and push the vented spike into the PP - container connection **[VIII]**.

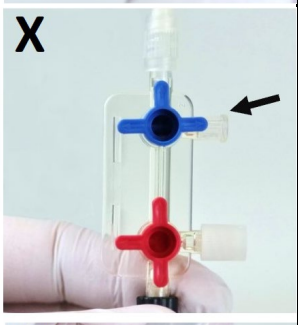


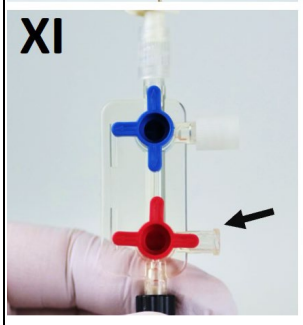


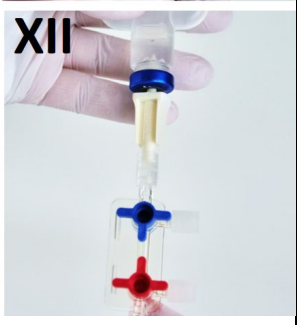
Now the air must be removed from the stopcock manifold and the attached inlet line. Be aware, that hydrochloric acid will thereby flow through and may drip out of the line and the side ports. Be prepared to remove the drops immediately.

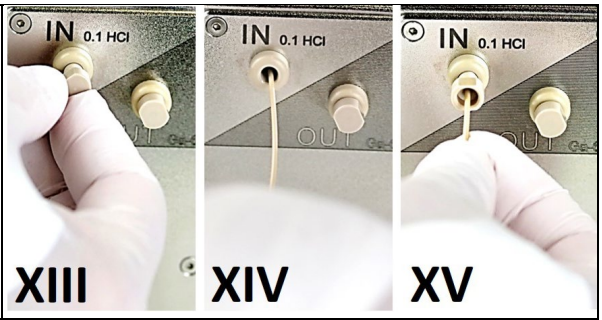
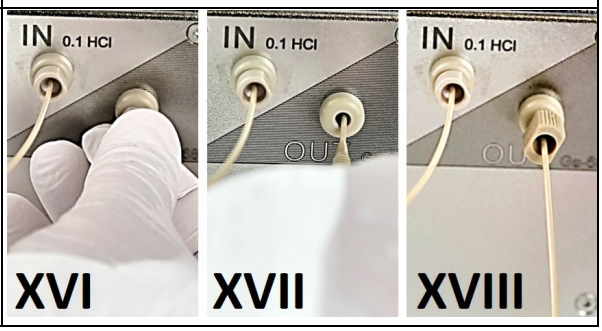
To remove the air, start by turning both valves of the stopcock manifold as shown in the picture **[IX]** (the prongs of both valves should be in the 6-9-12 clock position ┤). This will fill the inlet line with liquid and push the air out of it. Then turn the upper valve into the 9-12-3 clock position ⊥ and remove the cap of the upper side port to remove the air **[X]**. Afterwards, close the upper side port again with the cap. Now turn the upper valve back into the 6-9-12 clock position ┤ . Turn the lower valve into the 9-12-3 clock position ⊥ and remove the cap of the lower side port to remove the air **[XI]**. Close the lower side port again with the cap. Finally, place the upper valve into the 3-6-9 clock position ⊤ to stop flow of the liquid from the hydrochloric acid container **[XII]**.









4. Connecting the inlet line to the port of the radionuclide generator: Remove the plug from the inlet port of the radionuclide generator **[XIII].** To connect prepared and filled inlet line using the 1/16" M6 fingertight fitting, push the line into the inlet port **[XIV]** and screw in the fingertight fitting **[XV]**. Avoid hard bending or pinching of the line.	
5. Connecting the outlet line to the port of the radionuclide generator: Remove plug from the outlet port of the radionuclide generator **[XVI]**. To connect prepared outlet line using the 1/16" 10-32 fingertight fitting, push the line into the outlet port **[XVII]** and screw in the fingertight fitting **[XVIII]**. Avoid hard bending or pinching of the line.	

The radionuclide generator is now ready for the first elution:

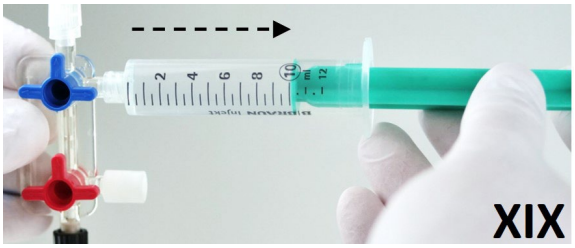


Please note: The radionuclide generator is designed not to drain itself, when no lines are connected to the inlet and outlet ports, but it is not recommended to leave the ports open at any time.
When the container with the sterile ultrapure 0.1 mol/l hydrochloric acid is connected and the fluid path is open, the radionuclide generator will be eluted by gravity. Therefore, it is necessary to keep the inlet and outlet lines as well as the positions of the stopcock valves under control.

First manual elution:

1. Prepare additional necessary materials:
   - Personal protective equipment: elutions should be performed while wearing eye and hand protection, and appropriate laboratory cloth.
   - Sterile syringe with 10 ml volume (avoid syringes with rubber plunger, preferably use two-piece syringes).
   - Shielded receiving vial or vessel with 10 ml or larger volume. Avoid uncoated stoppers as they may contain considerable amounts of zinc that is extracted by the acidic eluate.

2. Attach the syringe to the upper side port of the stopcock manifold and fill with 10 ml of sterile ultrapure 0.1 mol/l hydrochloric acid from the PP - container by turning the valve into the shown position, then moving the plunger of the syringe in the indicated direction while avoiding any air inside the syringe **[XIX]**.



3. Connect the shielded receiving vessel to the outlet line using the appropriate connector. The vessel must have sufficient capacity to accept the eluate volume. Avoid using metal syringe needles for connection.

4. Turn both valves of stopcock manifold towards the inlet port of the radionuclide generator. Push the 10 ml sterile ultrapure 0.1 mol/l hydrochloric acid at a flow rate not greater than 2 ml/minute **[XX]**. Eluting at a faster flow rate may reduce the shelf-life of the radionuclide generator. Five millilitres of eluent will fully elute the radionuclide generator, but for the first elution it is recommended to use 10 ml. If high resistance is encountered, do not force solution into radionuclide generator. If a peristaltic pump is used for elution, it should be set to a flow rate of not more than 2 ml/minute. The user should also verify that eluent is flowing without unusual resistance. If high resistance is noticed, discontinue elution.



CAUTION:
Be sure to introduce eluent through the inlet port; do not elute the radionuclide generator in reverse direction.
Elution efficiency (^{68}Ga yield) may be reduced if air is introduced into the radionuclide generator column.

5. Collect eluate in shielded receiving vessel and measure solution with a calibrated dose calibrator to determine the yield. If less than 5 ml of eluate have been collected, measurement may not represent the total potential yield of radionuclide generator. Please decay correct the measured activity to the starting time of the elution. For optimal yield of the radionuclide generator in its final position it is recommended to determine the elution peak by collecting small fractions of 0.5 ml.

6. The first eluate should be discarded due to the potential ^{68}Ge breakthrough in this eluate.

It is recommended to test the eluate for ^{68}Ge breakthrough after the first elutions by comparing the activity level of the ^{68}Ga and the ^{68}Ge. For further details please refer to Ph. Eur. monograph 2464.

Routine elution:

CAUTION:
Free ^{68}Ge ions can accumulate in the column over time. If the radionuclide generator has not been used for a period of 96 hours or more, the column should be pre-eluted once, at least 7 hours prior to eluting for radiolabelling. If the radiolabelling procedure does not require maximum achievable eluate activity, the time between the pre-elution and the elution for radiolabelling can be reduced (see also table 6 and calculation example below it). The pre-elution should be done using 10 ml of sterile ultrapure 0.1 mol/l hydrochloric acid.

1. Repeat the steps of the first elution but use only 5 ml eluent for the routine elution. The radionuclide generator is designed to elute all of the available ^{68}Ga activity in a volume of 5 ml.

2. The eluate is a clear, sterile, and colourless gallium (^{68}Ga) chloride solution, with a pH between 0.5 and 2.0 and a radiochemical purity greater than 95 %. Check the clarity of the eluate before use and discard it if the solution is not clear.

3. It is recommended to test the eluate for ^{68}Ge breakthrough during routine elutions by comparing the activity level of the ^{68}Ga and the ^{68}Ge. For further details please refer to Ph. Eur. monograph 2464.

CAUTION:
If fluid leaks are observed at any time, immediately stop eluting and attempt to contain the leaking fluid.

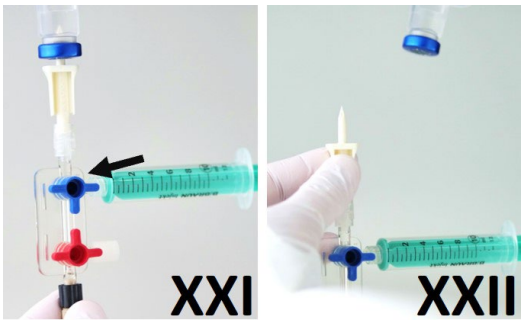
The radionuclide generator is supplied with 250 ml of sterile ultrapure 0.1 mol/l hydrochloric acid. This amount is usually sufficient for at least 40 elutions. The radionuclide generator should only be eluted with sterile ultrapure 0.1 mol/l hydrochloric acid supplied by the marketing authorisation holder. Additional containers may be purchased as consumables from the marketing authorisation holder only.

Exchange of sterile ultrapure 0.1 mol/l hydrochloric acid container:

CAUTION:
Aseptic technique is critical for maintenance of sterility and must be used during the exchange procedure.

1. When the sterile ultrapure 0.1 mol/l hydrochloric acid is almost consumed, the empty container can be replaced by a new sterile ultrapure 0.1 mol/l hydrochloric acid container.

   CAUTION:
   No air should enter the radionuclide generator. Before disconnecting the empty container, close all valves at the stopcock manifold and cap the side ports so that no air can enter into the manifold and spike **[XXI]**. Disconnect the container from the vented spike **[XXII]**. It is recommended to replace the vented spike with the new sterile vented spike supplied with each new sterile ultrapure 0.1 mol/l hydrochloric acid container.



2. Hang the new container with the 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid close to the inlet port above the radionuclide generator.

3. Push the connected vented spike into the container stopper; carefully check for air bubbles and slowly remove all air from the stopcock manifold using the valves. It is not necessary to detach the attached inlet line from the radionuclide generator or from the stopcock manifold. Entering of air into the radionuclide generator should be avoided.

4. When stopcock manifold is filled, close valves to stop flow. The radionuclide generator is now ready for elution again.

Radionuclide generator elution yield:

The activity stated on the label of the radionuclide generator is expressed in ^{68}Ge available at the calibration date (12:00 CET). The available ^{68}Ga activity depends on the ^{68}Ge activity at the time of elution and the elapsed time since the previous elution.

A radionuclide generator in full equilibrium yields more than 60 % of ^{68}Ga using an elution volume of 5 ml sterile ultrapure 0.1 mol/l hydrochloric acid.

The output will decrease with decay of the parent nuclide ^{68}Ge over time. For example, after 9 months' decay (39 weeks), the ^{68}Ge will be reduced by 50 % (see table 5). To calculate the current ^{68}Ge activity, multiply the ^{68}Ge activity at calibration date with the respective decay factor of the corresponding elapsed time in weeks.

Table 5: Decay Chart for ^{68}Ge

Elapsed Time in weeks	**Decay Factor**	**Elapsed Time in weeks**	**Decay Factor**
1	0.98	**27**	0.62
2	0.96	**28**	0.61
3	0.95	**29**	0.59
4	0.93	**30**	0.58
5	0.91	**31**	0.57
6	0.90	**32**	0.56
7	0.88	**33**	0.55
8	0.87	**34**	0.54
9	0.85	**35**	0.53
10	0.84	**36**	0.52
11	0.82	**37**	0.52
12	0.81	**38**	0.51
13	0.79	**39**	0.50
14	0.78	**40**	0.49
15	0.76	**41**	0.48
16	0.75	**42**	0.47
17	0.74	**43**	0.46
18	0.72	**44**	0.45
19	0.71	**45**	0.45
20	0.70	**46**	0.44
21	0.69	**47**	0.43
22	0.67	**48**	0.42
23	0.66	**49**	0.42
24	0.65	**50**	0.41
25	0.64	**51**	0.40
26	0.63	**52**	0.39

After elution, the ^{68}Ga will be built up by the continuous decay of the parent ^{68}Ge. The radionuclide generator requires at least 7 hours to achieve almost full yield after being eluted, but in practice it is also possible to elute the radionuclide generator earlier, depending on its strength and the activity required for radiolabelling. Table 6 shows the build-up factor of ^{68}Ga activity over time, up to 410 minutes after an elution.

Table 6: Build-up factors of ^{68}Ga

Elapsed Time in minutes	Build-Up Factor	Elapsed Time in minutes	Build-Up Factor
0	0.00	**210**	0.88
10	0.10	**220**	0.89
20	0.19	**230**	0.91
30	0.26	**240**	0.91
40	0.34	**250**	0.92
50	0.40	**260**	0.93
60	0.46	**270**	0.94
70	0.51	**280**	0.94
80	0.56	**290**	0.95
90	0.60	**300**	0.95
100	0.64	**310**	0.96
110	0.68	**320**	0.96
120	0.71	**330**	0.97
130	0.74	**340**	0.97
140	0.76	**350**	0.97
150	0.78	**360**	0.97
160	0.81	**370**	0.98
170	0.82	**380**	0.98
180	0.84	**390**	0.98
190	0.86	**400**	0.98
200	0.87	**410**	0.98

Calculation examples
A 1.85 GBq radionuclide generator is 12 weeks old. According to table 5, the activity of ^{68}Ge on the column can be calculated as follows:

1.85 GBq × 0.81 = 1.50 GBq

In full equilibrium, the activity of ^{68}Ga on the column is also 1.50 GBq.

The radionuclide generator is eluted and the collected ^{68}Ga activity is 1.05 GBq which corresponds to a yield of 70 %.

The same radionuclide generator is eluted 4 hours later. The 7 hours needed to reach the ^{68}Ge/^{68}Ga-equilibrium have not elapsed yet. The ^{68}Ga activity built up on the column in 4 hours (240 minutes) post-elution can be calculated according to table 6 as follows:

1.50 GBq × 0.91 = 1.37 GBq

With a typical yield of 70 % ^{68}Ga, the collected activity would then be:

1.37 GBq × 0.70 = 1.00 GBq

Note:
The activity of ^{68}Ga in the eluate can be measured to check the quality with regard to identity and content. The activity should be measured immediately after elution but may also be measured up to 5 half-life periods after elution.

Due to the short half-time of ^{68}Ga (67.71 minutes), the elapsed time between the elution and the measurement of the activity has to be decay-corrected to determine the actual yield at the elution time with the decay chart of ^{68}Ga, table 7.

Calculation Example
A new 1.85 GBq radionuclide generator is eluted. The activity of ^{68}Ga measured 10 minutes after the elution was 1.17 GBq.

The yield at the time of the elution can be obtained by dividing the measured activity by the corresponding decay factor of the elapsed time stated in table 7:
1.17 GBq / 0.90 = 1.30 GBq

This corresponds to a yield of ^{68}Ga of 70 % at the time of the elution:
1.30 GBq / 1.85 GBq × 100 % = 70 %

Table 7: Decay chart of ^{68}Ga

Elapsed Time in minutes	Decay Factor	Elapsed Time in minutes	Decay Factor
1	0.99	**35**	0.70
2	0.98	**36**	0.69
3	0.97	**37**	0.69
4	0.96	**38**	0.68
5	0.95	**39**	0.67
6	0.94	**40**	0.67
7	0.93	**41**	0.66
8	0.92	**42**	0.65
9	0.91	**43**	0.65
10	0.90	**44**	0.64
11	0.89	**45**	0.63
12	0.89	**46**	0.63
13	0.88	**47**	0.62
14	0.87	**48**	0.61
15	0.87	**49**	0.61
16	0.85	**50**	0.60
17	0.84	**51**	0.60
18	0.83	**52**	0.59
19	0.82	**53**	0.58
20	0.82	**54**	0.58
21	0.82	**55**	0.57
22	0.80	**56**	0.57
23	0.79	**57**	0.56
24	0.78	**58**	0.55
25	0.78	**59**	0.55
26	0.77	**60**	0.54
27	0.76	**61**	0.54
28	0.75	**62**	0.53
29	0.74	**63**	0.53
30	0.74	**64**	0.52
31	0.73	**65**	0.52
32	0.72	**66**	0.51
33	0.71	**67**	0.51
34	0.71	**68**	0.50

Quality control

If possible, clarity of the solution, pH and the radioactivity should be checked before radiolabelling.

^{68}Ge breakthrough

A small amount of ^{68}Ge is washed from the radionuclide generator column with each elution. ^{68}Ge breakthrough is expressed as a percentage of total ^{68}Ga activity eluted from the column, corrected for decay, and does not exceed 0.001 % of the eluted ^{68}Ga activity. ^{68}Ge breakthrough can, however, increase above 0.001 % if the radionuclide generator is not eluted for several days. Therefore, if the radionuclide generator has not been eluted for 96 hours or more, it should be pre-eluted with 10 ml of sterile ultrapure 0.1 mol/l hydrochloric acid at least 7 hours prior to the intended use (the time between the pre-elution and the elution for radiolabelling can be reduced if the intended radiolabelling procedure does not require maximum achievable eluate activity). When this instruction is followed, the ^{68}Ge breakthrough should constantly stay below 0.001 % in eluates obtained for radiolabelling. For testing the ^{68}Ge breakthrough, the activity levels of ^{68}Ga and ^{68}Ge in the eluate should be compared. For further details please refer to Ph. Eur. monograph 2464.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Detailed information on this medicinal product available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

RADIONUCLIDE GENERATOR

1. NAME OF THE MEDICINAL PRODUCT

GalliaPharm 1.11 GBq radionuclide generator

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride 1.11 GBq

3. LIST OF EXCIPIENTS

Column matrix: Titanium dioxide

Solution for elution: Sterile ultrapure 0.1 mol/l hydrochloric acid

4. PHARMACEUTICAL FORM AND CONTENTS

Radionuclide generator.

Germanium (^{68}Ge) activity at calibration date: {X.XX}

Elutable gallium (^{68}Ga) activity: > 60 % at equilibrium

Calibration date: {DD/MM/YYYY} (12:00 CET)

1. 1 x Container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid
2. 1 x Vented spike
3. 2 x Adapter 1/16" to male LUER
4. 2 x Tubing 60 cm
5. 1 x Tubing 40 cm
6. 1 x Tubing 20 cm
7. 3 x Fingertight fitting 1/16" 10-32
8. 1 x Fingertight fitting 1/16" M6
9. 1 x Stopcock manifold
10. 1 x Male LUER union

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For *in vitro* radiolabelling.

Not intended for direct use in patients.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Radiopharmaceutical



8. EXPIRY DATE

EXP {DD/MM/YYYY}

After elution, use eluate immediately.

9. SPECIAL STORAGE CONDITIONS

Do not dismantle the stainless-steel case.

Storage should be in accordance with national regulations for radioactive materials.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Read the package leaflet for instructions for use, handling, and disposal.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1836/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

RADIONUCLIDE GENERATOR

1. NAME OF THE MEDICINAL PRODUCT

GalliaPharm 1.48 GBq radionuclide generator

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride 1.48 GBq

3. LIST OF EXCIPIENTS

Column matrix: Titanium dioxide

Solution for elution: Sterile ultrapure 0.1 mol/l hydrochloric acid

4. PHARMACEUTICAL FORM AND CONTENTS

Radionuclide generator.

Germanium (^{68}Ge) activity at calibration date: {X.XX}

Elutable gallium (^{68}Ga) activity: > 60 % at equilibrium

Calibration date: {DD/MM/YYYY} (12:00 CET)

1. 1 x Container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid
2. 1 x Vented spike
3. 2 x Adapter 1/16" to male LUER
4. 2 x Tubing 60 cm
5. 1 x Tubing 40 cm
6. 1 x Tubing 20 cm
7. 3 x Fingertight fitting 1/16" 10-32
8. 1 x Fingertight fitting 1/16" M6
9. 1 x Stopcock manifold
10. 1 x Male LUER union

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For *in vitro* radiolabelling.

Not intended for direct use in patients.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Radiopharmaceutical



8. EXPIRY DATE

EXP {DD/MM/YYYY}

After elution, use eluate immediately.

9. SPECIAL STORAGE CONDITIONS

Do not dismantle the stainless-steel case.

Storage should be in accordance with national regulations for radioactive materials.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Read the package leaflet for instructions for use, handling, and disposal.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1836/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

RADIONUCLIDE GENERATOR

1. NAME OF THE MEDICINAL PRODUCT

GalliaPharm 1.85 GBq radionuclide generator

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride 1.85 GBq

3. LIST OF EXCIPIENTS

Column matrix: Titanium dioxide

Solution for elution: Sterile ultrapure 0.1 mol/l hydrochloric acid

4. PHARMACEUTICAL FORM AND CONTENTS

Radionuclide generator.

Germanium (^{68}Ge) activity at calibration date: {X.XX}

Elutable gallium (^{68}Ga) activity: > 60 % at equilibrium

Calibration date: {DD/MM/YYYY} (12:00 CET)

1. 1 x Container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid
2. 1 x Vented spike
3. 2 x Adapter 1/16" to male LUER
4. 2 x Tubing 60 cm
5. 1 x Tubing 40 cm
6. 1 x Tubing 20 cm
7. 3 x Fingertight fitting 1/16" 10-32
8. 1 x Fingertight fitting 1/16" M6
9. 1 x Stopcock manifold
10. 1 x Male LUER union

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For *in vitro* radiolabelling.

Not intended for direct use in patients.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Radiopharmaceutical



8. EXPIRY DATE

EXP {DD/MM/YYYY}

After elution, use eluate immediately.

9. SPECIAL STORAGE CONDITIONS

Do not dismantle the stainless-steel case.

Storage should be in accordance with national regulations for radioactive materials.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Read the package leaflet for instructions for use, handling, and disposal.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1836/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

RADIONUCLIDE GENERATOR

1. NAME OF THE MEDICINAL PRODUCT

GalliaPharm 2.22 GBq radionuclide generator

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride 2.22 GBq

3. LIST OF EXCIPIENTS

Column matrix: Titanium dioxide

Solution for elution: Sterile ultrapure 0.1 mol/l hydrochloric acid

4. PHARMACEUTICAL FORM AND CONTENTS

Radionuclide generator.

Germanium (^{68}Ge) activity at calibration date: {X.XX}

Elutable gallium (^{68}Ga) activity: > 60 % at equilibrium

Calibration date: {DD/MM/YYYY} (12:00 CET)

1. 1 x Container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid
2. 1 x Vented spike
3. 2 x Adapter 1/16" to male LUER
4. 2 x Tubing 60 cm
5. 1 x Tubing 40 cm
6. 1 x Tubing 20 cm
7. 3 x Fingertight fitting 1/16" 10-32
8. 1 x Fingertight fitting 1/16" M6
9. 1 x Stopcock manifold
10. 1 x Male LUER union

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For *in vitro* radiolabelling.

Not intended for direct use in patients.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Radiopharmaceutical



8. EXPIRY DATE

EXP {DD/MM/YYYY}

After elution, use eluate immediately.

9. SPECIAL STORAGE CONDITIONS

Do not dismantle the stainless-steel case.

Storage should be in accordance with national regulations for radioactive materials.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Read the package leaflet for instructions for use, handling, and disposal.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1836/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

RADIONUCLIDE GENERATOR

1. NAME OF THE MEDICINAL PRODUCT

GalliaPharm 2.59 GBq radionuclide generator

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride 2.59 GBq

3. LIST OF EXCIPIENTS

Column matrix: Titanium dioxide

Solution for elution: Sterile ultrapure 0.1 mol/l hydrochloric acid

4. PHARMACEUTICAL FORM AND CONTENTS

Radionuclide generator.

Germanium (^{68}Ge) activity at calibration date: {X.XX}

Elutable gallium (^{68}Ga) activity: > 60 % at equilibrium

Calibration date: {DD/MM/YYYY} (12:00 CET)

1. 1 x Container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid
2. 1 x Vented spike
3. 2 x Adapter 1/16" to male LUER
4. 2 x Tubing 60 cm
5. 1 x Tubing 40 cm
6. 1 x Tubing 20 cm
7. 3 x Fingertight fitting 1/16" 10-32
8. 1 x Fingertight fitting 1/16" M6
9. 1 x Stopcock manifold
10. 1 x Male LUER union

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For *in vitro* radiolabelling.

Not intended for direct use in patients.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Radiopharmaceutical



8. EXPIRY DATE

EXP {DD/MM/YYYY}

After elution, use eluate immediately.

9. SPECIAL STORAGE CONDITIONS

Do not dismantle the stainless-steel case.

Storage should be in accordance with national regulations for radioactive materials.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Read the package leaflet for instructions for use, handling, and disposal.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1836/005

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

RADIONUCLIDE GENERATOR

1. NAME OF THE MEDICINAL PRODUCT

GalliaPharm 2.96 GBq radionuclide generator

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride 2.96 GBq

3. LIST OF EXCIPIENTS

Column matrix: Titanium dioxide

Solution for elution: Sterile ultrapure 0.1 mol/l hydrochloric acid

4. PHARMACEUTICAL FORM AND CONTENTS

Radionuclide generator.

Germanium (^{68}Ge) activity at calibration date: {X.XX}

Elutable gallium (^{68}Ga) activity: > 60 % at equilibrium

Calibration date: {DD/MM/YYYY} (12:00 CET)

1. 1 x Container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid
2. 1 x Vented spike
3. 2 x Adapter 1/16" to male LUER
4. 2 x Tubing 60 cm
5. 1 x Tubing 40 cm
6. 1 x Tubing 20 cm
7. 3 x Fingertight fitting 1/16" 10-32
8. 1 x Fingertight fitting 1/16" M6
9. 1 x Stopcock manifold
10. 1 x Male LUER union

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For *in vitro* radiolabelling.

Not intended for direct use in patients.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Radiopharmaceutical



8. EXPIRY DATE

EXP {DD/MM/YYYY}

After elution, use eluate immediately.

9. SPECIAL STORAGE CONDITIONS

Do not dismantle the stainless-steel case.

Storage should be in accordance with national regulations for radioactive materials.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Read the package leaflet for instructions for use, handling, and disposal.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1836/006

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

RADIONUCLIDE GENERATOR

1. NAME OF THE MEDICINAL PRODUCT

GalliaPharm 3.33 GBq radionuclide generator

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride 3.33 GBq

3. LIST OF EXCIPIENTS

Column matrix: Titanium dioxide

Solution for elution: Sterile ultrapure 0.1 mol/l hydrochloric acid

4. PHARMACEUTICAL FORM AND CONTENTS

Radionuclide generator.

Germanium (^{68}Ge) activity at calibration date: {X.XX}

Elutable gallium (^{68}Ga) activity: > 60 % at equilibrium

Calibration date: {DD/MM/YYYY} (12:00 CET)

1. 1 x Container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid
2. 1 x Vented spike
3. 2 x Adapter 1/16" to male LUER
4. 2 x Tubing 60 cm
5. 1 x Tubing 40 cm
6. 1 x Tubing 20 cm
7. 3 x Fingertight fitting 1/16" 10-32
8. 1 x Fingertight fitting 1/16" M6
9. 1 x Stopcock manifold
10. 1 x Male LUER union

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For *in vitro* radiolabelling.

Not intended for direct use in patients.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Radiopharmaceutical



8. EXPIRY DATE

EXP {DD/MM/YYYY}

After elution, use eluate immediately.

9. SPECIAL STORAGE CONDITIONS

Do not dismantle the stainless-steel case.

Storage should be in accordance with national regulations for radioactive materials.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Read the package leaflet for instructions for use, handling, and disposal.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1836/007

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

RADIONUCLIDE GENERATOR

1. NAME OF THE MEDICINAL PRODUCT

GalliaPharm 3.70 GBq radionuclide generator

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

germanium (^{68}Ge) chloride / gallium (^{68}Ga) chloride 3.70 GBq

3. LIST OF EXCIPIENTS

Column matrix: Titanium dioxide

Solution for elution: Sterile ultrapure 0.1 mol/l hydrochloric acid

4. PHARMACEUTICAL FORM AND CONTENTS

Radionuclide generator.

Germanium (^{68}Ge) activity at calibration date: {X.XX}

Elutable gallium (^{68}Ga) activity: > 60 % at equilibrium

Calibration date: {DD/MM/YYYY} (12:00 CET)

1. 1 x Container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid
2. 1 x Vented spike
3. 2 x Adapter 1/16" to male LUER
4. 2 x Tubing 60 cm
5. 1 x Tubing 40 cm
6. 1 x Tubing 20 cm
7. 3 x Fingertight fitting 1/16" 10-32
8. 1 x Fingertight fitting 1/16" M6
9. 1 x Stopcock manifold
10. 1 x Male LUER union

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For *in vitro* radiolabelling.

Not intended for direct use in patients.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Radiopharmaceutical



8. EXPIRY DATE

EXP {DD/MM/YYYY}

After elution, use eluate immediately.

9. SPECIAL STORAGE CONDITIONS

Do not dismantle the stainless-steel case.

Storage should be in accordance with national regulations for radioactive materials.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Read the package leaflet for instructions for use, handling, and disposal.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1836/008

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

COLUMN INSIDE THE RADIONUCLIDE GENERATOR

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

4. BATCH NUMBER

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

Ge-68/Ga-68



PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

STERILE ULTRAPURE 0.1 MOL/L HYDROCHLORIC ACID – OUTER AND INNER PACKAGING

1. NAME OF THE MEDICINAL PRODUCT

Solvent for GalliaPharm

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Hydrochloric acid (0.1 mol/l)

3. LIST OF EXCIPIENTS

Water

4. PHARMACEUTICAL FORM AND CONTENTS

Solvent for GalliaPharm

250 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For elution of the radionuclide generator.

Not intended for direct use in patients.

Read package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Read the package leaflet for instructions for use, handling, and disposal.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin, Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1836/001-008

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

Read the package leaflet for instructions for use, handling, and disposal.

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

GalliaPharm 1.11 GBq radionuclide generator

Gallium (^{68}Ga) chloride solution

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What GalliaPharm is and what it is used for
2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
3. How gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
4. Possible side effects
5. How GalliaPharm is stored
6. Contents of the pack and other information

1. What GalliaPharm is and what it is used for

GalliaPharm is a germanium (^{68}Ge)/gallium (^{68}Ga) radionuclide generator, a device used to obtain a solution of gallium (^{68}Ga) chloride. Gallium (^{68}Ga) chloride is a radioactive substance that is handled by specialised doctors (nuclear medicine doctors) and pharmacists trained to work with radioactive materials. Gallium (^{68}Ga) chloride is not intended for direct use in patients, but is used for radiolabelling, a technique in which a substance is tagged (radiolabelled) with a radioactive compound, here ^{68}Ga.

Only medicines that have been specifically developed and approved for radiolabelling with ^{68}Ga undergo the radiolabelling procedure with gallium (^{68}Ga) chloride. These radiolabelled medicines can recognise and attach to particular types of cells in the body and take the radioactive ^{68}Ga to these cells in your body. The low amount of radioactivity present in the ^{68}Ga-labelled medicine can be detected from outside of the body by special cameras. This may help your doctor with the diagnosis. Please refer to the Package Leaflet of the medicine that is to be radiolabelled with gallium (^{68}Ga) chloride for more information.

The nuclear medicine doctor will explain to you in more detail what type of examination will be performed.

The use of a ^{68}Ga-labelled medicine does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the ^{68}Ga-labelled medicine overcomes the risk due to radiation.

2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must not be used

- if you are allergic to gallium (^{68}Ga) chloride or any of the other ingredients of this medicine (listed in section 6).

If you are using a ^{68}Ga-labelled medicine, you should read information on contraindications in the Package Leaflet of the medicine to be radiolabelled.

Warnings and precautions
For information concerning special warnings and special precautions for use of ^{68}Ga-labelled medicines please refer to the Package Leaflet of the medicine to be radiolabelled.

Children and adolescents
Please speak to your nuclear medicine doctor if you or your child are under 18 years old.

Other medicines and gallium (^{68}Ga) chloride solution
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines since they may interfere with the interpretation of the images by your doctor.

It is not known whether gallium (^{68}Ga) chloride solution may interact with other medicines as specified studies have not been carried out. You will not receive an injection of gallium (^{68}Ga) chloride, but a medicine radiolabelled with ^{68}Ga.

For information concerning other medicines in combination with the use of ^{68}Ga-labelled medicines, please read the Package Leaflet of the radiolabelled medicine.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your nuclear medicine doctor for advice before you are given ^{68}Ga-labelled medicines.

You must inform the nuclear medicine doctor before the administration of ^{68}Ga-labelled medicines if there is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding.

When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

<u>If you are pregnant</u>
The nuclear medicine doctor will only administer a ^{68}Ga-labelled medicine during pregnancy if a benefit is expected which would outweigh the risks.

<u>If you are breast-feeding</u>
You will be asked to stop breast-feeding. Please ask your nuclear medicine doctor when you can resume breast-feeding.

Driving and using machines
There could be effects on your ability to drive and to use machines due to the use of ^{68}Ga-labelled medicines. Please read the Package Leaflets of these medicines carefully.

3. How gallium (^{68}Ga) chloride solution produced with GalliaPharm is used

There are strict laws on the use, handling, and disposal of radiopharmaceutical products. GalliaPharm will only be used in special controlled areas. The production of gallium (^{68}Ga) chloride solution, radiolabelling of a specific carrier medicine, as well as administration of ^{68}Ga-labelled medicine to you, will only be handled by people who are trained and qualified to use it safely. They will take special care for the safe use of this medicine and will keep you informed of their actions.

The nuclear medicine doctor supervising the procedure will decide on the amount of medicine radiolabelled with ^{68}Ga to be used in your case. It will be the smallest quantity necessary to achieve the appropriate outcome.

Administration of gallium (^{68}Ga) chloride solution and conduct of the procedure
You will not be given the gallium (^{68}Ga) chloride solution, but another medicine which has been combined (radiolabelled) with gallium (^{68}Ga) chloride solution.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure with a ^{68}Ga-labelled medicine. For more information, please read the Package Leaflet of the radiolabelled medicine.

After the medicine radiolabelled with gallium (^{68}Ga) chloride solution has been given
The nuclear medicine doctor will inform you if you need to take any special precautions after receiving the ^{68}Ga-labelled medicine. Contact your nuclear medicine doctor if you have any questions.

If you have been given more medicine radiolabelled with gallium (^{68}Ga) chloride solution than you should, or have received direct injection of gallium (^{68}Ga) chloride solution inadvertently
An overdose, or inadvertent direct injection of gallium (^{68}Ga) chloride solution is unlikely, because you will only receive the ^{68}Ga-labelled medicine precisely controlled by the nuclear medicine doctor supervising the procedure. However, in the case of an overdose, or inadvertent direct injection you will receive the appropriate care.

Should you have any further questions on the use of this medicine, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, the ^{68}Ga-labelled medicine can cause side effects, although not everybody gets them.

After the ^{68}Ga-labelled medicine is administered, it will deliver low amounts of ionising radiation with the least risk of cancer and hereditary abnormalities.

For more information about possible side effects, please read the Package Leaflet of the radiolabelled medicine.

Reporting of side effects
If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How GalliaPharm is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

The following information is intended for the specialist only.

The radionuclide generator must not be used after the expiry date stated on the container after "EXP".

Do not dismantle the case.

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must be used immediately.

6. Contents of the pack and other information

What GalliaPharm contains

- The active substance consists of germanium (^{68}Ge) chloride and gallium (^{68}Ga) chloride dissolved in sterile ultrapure 0.1 mol/l hydrochloric acid. Germanium (^{68}Ge) is irreversibly trapped inside the radionuclide generator decaying to its daughter nuclide (^{68}Ga), which is obtained from the generator as gallium (^{68}Ga) chloride.
- The other ingredients are: Titanium dioxide (matrix)
  Sterile ultrapure 0.1 mol/l hydrochloric acid (solution for elution)

One radionuclide generator is supplied with:

1. 1 x PP – container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid (including a separate hanger for PP-bottles; PP = Polypropylene)
2. 1 x Vented spike (ABS = Acrylonitrile Butadiene Styrene/PE = Polyethylene)
3. 2 x Adapter 1/16" to male LUER (PEEK)
4. 2 x Tubing 60 cm (PEEK)
5. 1 x Tubing 40 cm (PEEK)
6. 1 x Tubing 20 cm (PEEK)
7. 3 x Fingertight fitting 1/16" 10-32 (PEEK)
8. 1 x Fingertight fitting 1/16" M6 (PEEK)
9. 1 x Stopcock manifold (TPX = Polymethylpentene/HDPE = High Density Polyethylene)
10. 1 x Male LUER union (PP)

What GalliaPharm looks like and contents of the pack
You will not need to obtain or handle this medicine.

Marketing Authorisation Holder and Manufacturer
Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

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The following information is intended for healthcare professionals only:

The complete SmPC of GalliaPharm is provided as a separate document in the product package, with the objective to provide healthcare professionals with other additional scientific and practical information about the administration and use of this radiopharmaceutical.

Please refer to the SmPC.

Package leaflet: Information for the patient

GalliaPharm 1.48 GBq radionuclide generator

Gallium (^{68}Ga) chloride solution

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What GalliaPharm is and what it is used for
2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
3. How gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
4. Possible side effects
5. How GalliaPharm is stored
6. Contents of the pack and other information

1. What GalliaPharm is and what it is used for

GalliaPharm is a germanium (^{68}Ge)/gallium (^{68}Ga) radionuclide generator, a device used to obtain a solution of gallium (^{68}Ga) chloride. Gallium (^{68}Ga) chloride is a radioactive substance that is handled by specialised doctors (nuclear medicine doctors) and pharmacists trained to work with radioactive materials. Gallium (^{68}Ga) chloride is not intended for direct use in patients, but is used for radiolabelling, a technique in which a substance is tagged (radiolabelled) with a radioactive compound, here ^{68}Ga.

Only medicines that have been specifically developed and approved for radiolabelling with ^{68}Ga undergo the radiolabelling procedure with gallium (^{68}Ga) chloride. These radiolabelled medicines can recognise and attach to particular types of cells in the body and take the radioactive ^{68}Ga to these cells in your body. The low amount of radioactivity present in the ^{68}Ga-labelled medicine can be detected from outside of the body by special cameras. This may help your doctor with the diagnosis. Please refer to the Package Leaflet of the medicine that is to be radiolabelled with gallium (^{68}Ga) chloride for more information.

The nuclear medicine doctor will explain to you in more detail what type of examination will be performed.

The use of a ^{68}Ga-labelled medicine does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the ^{68}Ga-labelled medicine overcomes the risk due to radiation.

2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must not be used

- if you are allergic to gallium (^{68}Ga) chloride or any of the other ingredients of this medicine (listed in section 6).

If you are using a ^{68}Ga-labelled medicine, you should read information on contraindications in the Package Leaflet of the medicine to be radiolabelled.

Warnings and precautions
For information concerning special warnings and special precautions for use of ^{68}Ga-labelled medicines please refer to the Package Leaflet of the medicine to be radiolabelled.

Children and adolescents
Please speak to your nuclear medicine doctor if you or your child are under 18 years old.

Other medicines and gallium (^{68}Ga) chloride solution
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines since they may interfere with the interpretation of the images by your doctor.

It is not known whether gallium (^{68}Ga) chloride solution may interact with other medicines as specified studies have not been carried out. You will not receive an injection of gallium (^{68}Ga) chloride, but a medicine radiolabelled with ^{68}Ga.

For information concerning other medicines in combination with the use of ^{68}Ga-labelled medicines, please read the Package Leaflet of the radiolabelled medicine.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your nuclear medicine doctor for advice before you are given ^{68}Ga-labelled medicines.

You must inform the nuclear medicine doctor before the administration of ^{68}Ga-labelled medicines if there is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding.

When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

<u>If you are pregnant</u>
The nuclear medicine doctor will only administer a ^{68}Ga-labelled medicine during pregnancy if a benefit is expected which would outweigh the risks.

<u>If you are breast-feeding</u>
You will be asked to stop breast-feeding. Please ask your nuclear medicine doctor when you can resume breast-feeding.

Driving and using machines
There could be effects on your ability to drive and to use machines due to the use of ^{68}Ga-labelled medicines. Please read the Package Leaflets of these medicines carefully.

3. How gallium (^{68}Ga) chloride solution produced with GalliaPharm is used

There are strict laws on the use, handling, and disposal of radiopharmaceutical products. GalliaPharm will only be used in special controlled areas. The production of gallium (^{68}Ga) chloride solution, radiolabelling of a specific carrier medicine, as well as administration of ^{68}Ga-labelled medicine to you, will only be handled by people who are trained and qualified to use it safely. They will take special care for the safe use of this medicine and will keep you informed of their actions.

The nuclear medicine doctor supervising the procedure will decide on the amount of medicine radiolabelled with ^{68}Ga to be used in your case. It will be the smallest quantity necessary to achieve the appropriate outcome.

Administration of gallium (^{68}Ga) chloride solution and conduct of the procedure
You will not be given the gallium (^{68}Ga) chloride solution, but another medicine which has been combined (radiolabelled) with gallium (^{68}Ga) chloride solution.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure with a ^{68}Ga-labelled medicine. For more information, please read the Package Leaflet of the radiolabelled medicine.

After the medicine radiolabelled with gallium (^{68}Ga) chloride solution has been given
The nuclear medicine doctor will inform you if you need to take any special precautions after receiving the ^{68}Ga-labelled medicine. Contact your nuclear medicine doctor if you have any questions.

If you have been given more medicine radiolabelled with gallium (^{68}Ga) chloride solution than you should, or have received direct injection of gallium (^{68}Ga) chloride solution inadvertently
An overdose, or inadvertent direct injection of gallium (^{68}Ga) chloride solution is unlikely, because you will only receive the ^{68}Ga-labelled medicine precisely controlled by the nuclear medicine doctor supervising the procedure. However, in the case of an overdose, or inadvertent direct injection you will receive the appropriate care.

Should you have any further questions on the use of this medicine, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, the ^{68}Ga-labelled medicine can cause side effects, although not everybody gets them.

After the ^{68}Ga-labelled medicine is administered, it will deliver low amounts of ionising radiation with the least risk of cancer and hereditary abnormalities.

For more information about possible side effects, please read the Package Leaflet of the radiolabelled medicine.

Reporting of side effects
If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How GalliaPharm is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

The following information is intended for the specialist only.

The radionuclide generator must not be used after the expiry date stated on the container after "EXP".

Do not dismantle the case.

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must be used immediately.

6. Contents of the pack and other information

What GalliaPharm contains

- The active substance consists of germanium (^{68}Ge) chloride and gallium (^{68}Ga) chloride dissolved in sterile ultrapure 0.1 mol/l hydrochloric acid. Germanium (^{68}Ge) is irreversibly trapped inside the radionuclide generator decaying to its daughter nuclide (^{68}Ga), which is obtained from the generator as gallium (^{68}Ga) chloride.
- The other ingredients are: Titanium dioxide (matrix)
  Sterile ultrapure 0.1 mol/l hydrochloric acid (solution for elution)

One radionuclide generator is supplied with:

1. 1 x PP – container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid (including a separate hanger for PP-bottles; PP = Polypropylene)
2. 1 x Vented spike (ABS = Acrylonitrile Butadiene Styrene/PE = Polyethylene)
3. 2 x Adapter 1/16" to male LUER (PEEK)
4. 2 x Tubing 60 cm (PEEK)
5. 1 x Tubing 40 cm (PEEK)
6. 1 x Tubing 20 cm (PEEK)
7. 3 x Fingertight fitting 1/16" 10-32 (PEEK)
8. 1 x Fingertight fitting 1/16" M6 (PEEK)
9. 1 x Stopcock manifold (TPX = Polymethylpentene/HDPE = High Density Polyethylene)
10. 1 x Male LUER union (PP)

What GalliaPharm looks like and contents of the pack
You will not need to obtain or handle this medicine.

Marketing Authorisation Holder and Manufacturer
Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

This leaflet was last revised in.

Other sources of information

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This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

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The following information is intended for healthcare professionals only:

The complete SmPC of GalliaPharm is provided as a separate document in the product package, with the objective to provide healthcare professionals with other additional scientific and practical information about the administration and use of this radiopharmaceutical.

Please refer to the SmPC.

Package leaflet: Information for the patient

GalliaPharm 1.85 GBq radionuclide generator

Gallium (^{68}Ga) chloride solution

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What GalliaPharm is and what it is used for
2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
3. How gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
4. Possible side effects
5. How GalliaPharm is stored
6. Contents of the pack and other information

1. What GalliaPharm is and what it is used for

GalliaPharm is a germanium (^{68}Ge)/gallium (^{68}Ga) radionuclide generator, a device used to obtain a solution of gallium (^{68}Ga) chloride. Gallium (^{68}Ga) chloride is a radioactive substance that is handled by specialised doctors (nuclear medicine doctors) and pharmacists trained to work with radioactive materials. Gallium (^{68}Ga) chloride is not intended for direct use in patients, but is used for radiolabelling, a technique in which a substance is tagged (radiolabelled) with a radioactive compound, here ^{68}Ga.

Only medicines that have been specifically developed and approved for radiolabelling with ^{68}Ga undergo the radiolabelling procedure with gallium (^{68}Ga) chloride. These radiolabelled medicines can recognise and attach to particular types of cells in the body and take the radioactive ^{68}Ga to these cells in your body. The low amount of radioactivity present in the ^{68}Ga-labelled medicine can be detected from outside of the body by special cameras. This may help your doctor with the diagnosis. Please refer to the Package Leaflet of the medicine that is to be radiolabelled with gallium (^{68}Ga) chloride for more information.

The nuclear medicine doctor will explain to you in more detail what type of examination will be performed.

The use of a ^{68}Ga-labelled medicine does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the ^{68}Ga-labelled medicine overcomes the risk due to radiation.

2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must not be used

- if you are allergic to gallium (^{68}Ga) chloride or any of the other ingredients of this medicine (listed in section 6).

If you are using a ^{68}Ga-labelled medicine, you should read information on contraindications in the Package Leaflet of the medicine to be radiolabelled.

Warnings and precautions
For information concerning special warnings and special precautions for use of ^{68}Ga-labelled medicines please refer to the Package Leaflet of the medicine to be radiolabelled.

Children and adolescents
Please speak to your nuclear medicine doctor if you or your child are under 18 years old.

Other medicines and gallium (^{68}Ga) chloride solution
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines since they may interfere with the interpretation of the images by your doctor.

It is not known whether gallium (^{68}Ga) chloride solution may interact with other medicines as specified studies have not been carried out. You will not receive an injection of gallium (^{68}Ga) chloride, but a medicine radiolabelled with ^{68}Ga.

For information concerning other medicines in combination with the use of ^{68}Ga-labelled medicines, please read the Package Leaflet of the radiolabelled medicine.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your nuclear medicine doctor for advice before you are given ^{68}Ga-labelled medicines.

You must inform the nuclear medicine doctor before the administration of ^{68}Ga-labelled medicines if there is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding.

When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

<u>If you are pregnant</u>
The nuclear medicine doctor will only administer a ^{68}Ga-labelled medicine during pregnancy if a benefit is expected which would outweigh the risks.

<u>If you are breast-feeding</u>
You will be asked to stop breast-feeding. Please ask your nuclear medicine doctor when you can resume breast-feeding.

Driving and using machines
There could be effects on your ability to drive and to use machines due to the use of ^{68}Ga-labelled medicines. Please read the Package Leaflets of these medicines carefully.

3. How gallium (^{68}Ga) chloride solution produced with GalliaPharm is used

There are strict laws on the use, handling, and disposal of radiopharmaceutical products. GalliaPharm will only be used in special controlled areas. The production of gallium (^{68}Ga) chloride solution, radiolabelling of a specific carrier medicine, as well as administration of ^{68}Ga-labelled medicine to you, will only be handled by people who are trained and qualified to use it safely. They will take special care for the safe use of this medicine and will keep you informed of their actions.

The nuclear medicine doctor supervising the procedure will decide on the amount of medicine radiolabelled with ^{68}Ga to be used in your case. It will be the smallest quantity necessary to achieve the appropriate outcome.

Administration of gallium (^{68}Ga) chloride solution and conduct of the procedure
You will not be given the gallium (^{68}Ga) chloride solution, but another medicine which has been combined (radiolabelled) with gallium (^{68}Ga) chloride solution.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure with a ^{68}Ga-labelled medicine. For more information, please read the Package Leaflet of the radiolabelled medicine.

After the medicine radiolabelled with gallium (^{68}Ga) chloride solution has been given
The nuclear medicine doctor will inform you if you need to take any special precautions after receiving the ^{68}Ga-labelled medicine. Contact your nuclear medicine doctor if you have any questions.

If you have been given more medicine radiolabelled with gallium (^{68}Ga) chloride solution than you should, or have received direct injection of gallium (^{68}Ga) chloride solution inadvertently
An overdose, or inadvertent direct injection of gallium (^{68}Ga) chloride solution is unlikely, because you will only receive the ^{68}Ga-labelled medicine precisely controlled by the nuclear medicine doctor supervising the procedure. However, in the case of an overdose, or inadvertent direct injection you will receive the appropriate care.

Should you have any further questions on the use of this medicine, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, the ^{68}Ga-labelled medicine can cause side effects, although not everybody gets them.

After the ^{68}Ga-labelled medicine is administered, it will deliver low amounts of ionising radiation with the least risk of cancer and hereditary abnormalities.

For more information about possible side effects, please read the Package Leaflet of the radiolabelled medicine.

Reporting of side effects
If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How GalliaPharm is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

The following information is intended for the specialist only.

The radionuclide generator must not be used after the expiry date stated on the container after "EXP".

Do not dismantle the case.

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must be used immediately.

6. Contents of the pack and other information

What GalliaPharm contains

- The active substance consists of germanium (^{68}Ge) chloride and gallium (^{68}Ga) chloride dissolved in sterile ultrapure 0.1 mol/l hydrochloric acid. Germanium (^{68}Ge) is irreversibly trapped inside the radionuclide generator decaying to its daughter nuclide (^{68}Ga), which is obtained from the generator as gallium (^{68}Ga) chloride.
- The other ingredients are: Titanium dioxide (matrix)
  Sterile ultrapure 0.1 mol/l hydrochloric acid (solution for elution)

One radionuclide generator is supplied with:

1. 1 x PP – container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid (including a separate hanger for PP-bottles; PP = Polypropylene)
2. 1 x Vented spike (ABS = Acrylonitrile Butadiene Styrene/PE = Polyethylene)
3. 2 x Adapter 1/16" to male LUER (PEEK)
4. 2 x Tubing 60 cm (PEEK)
5. 1 x Tubing 40 cm (PEEK)
6. 1 x Tubing 20 cm (PEEK)
7. 3 x Fingertight fitting 1/16" 10-32 (PEEK)
8. 1 x Fingertight fitting 1/16" M6 (PEEK)
9. 1 x Stopcock manifold (TPX = Polymethylpentene/HDPE = High Density Polyethylene)
10. 1 x Male LUER union (PP)

What GalliaPharm looks like and contents of the pack
You will not need to obtain or handle this medicine.

Marketing Authorisation Holder and Manufacturer
Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

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The complete SmPC of GalliaPharm is provided as a separate document in the product package, with the objective to provide healthcare professionals with other additional scientific and practical information about the administration and use of this radiopharmaceutical.

Please refer to the SmPC.

Package leaflet: Information for the patient

GalliaPharm 2.22 GBq radionuclide generator

Gallium (^{68}Ga) chloride solution

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What GalliaPharm is and what it is used for
2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
3. How gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
4. Possible side effects
5. How GalliaPharm is stored
6. Contents of the pack and other information

1. What GalliaPharm is and what it is used for

GalliaPharm is a germanium (^{68}Ge)/gallium (^{68}Ga) radionuclide generator, a device used to obtain a solution of gallium (^{68}Ga) chloride. Gallium (^{68}Ga) chloride is a radioactive substance that is handled by specialised doctors (nuclear medicine doctors) and pharmacists trained to work with radioactive materials. Gallium (^{68}Ga) chloride is not intended for direct use in patients, but is used for radiolabelling, a technique in which a substance is tagged (radiolabelled) with a radioactive compound, here ^{68}Ga.

Only medicines that have been specifically developed and approved for radiolabelling with ^{68}Ga undergo the radiolabelling procedure with gallium (^{68}Ga) chloride. These radiolabelled medicines can recognise and attach to particular types of cells in the body and take the radioactive ^{68}Ga to these cells in your body. The low amount of radioactivity present in the ^{68}Ga-labelled medicine can be detected from outside of the body by special cameras. This may help your doctor with the diagnosis. Please refer to the Package Leaflet of the medicine that is to be radiolabelled with gallium (^{68}Ga) chloride for more information.

The nuclear medicine doctor will explain to you in more detail what type of examination will be performed.

The use of a ^{68}Ga-labelled medicine does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the ^{68}Ga-labelled medicine overcomes the risk due to radiation.

2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must not be used

- if you are allergic to gallium (^{68}Ga) chloride or any of the other ingredients of this medicine (listed in section 6).

If you are using a ^{68}Ga-labelled medicine, you should read information on contraindications in the Package Leaflet of the medicine to be radiolabelled.

Warnings and precautions
For information concerning special warnings and special precautions for use of ^{68}Ga-labelled medicines please refer to the Package Leaflet of the medicine to be radiolabelled.

Children and adolescents
Please speak to your nuclear medicine doctor if you or your child are under 18 years old.

Other medicines and gallium (^{68}Ga) chloride solution
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines since they may interfere with the interpretation of the images by your doctor.

It is not known whether gallium (^{68}Ga) chloride solution may interact with other medicines as specified studies have not been carried out. You will not receive an injection of gallium (^{68}Ga) chloride, but a medicine radiolabelled with ^{68}Ga.

For information concerning other medicines in combination with the use of ^{68}Ga-labelled medicines, please read the Package Leaflet of the radiolabelled medicine.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your nuclear medicine doctor for advice before you are given ^{68}Ga-labelled medicines.

You must inform the nuclear medicine doctor before the administration of ^{68}Ga-labelled medicines if there is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding.

When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

<u>If you are pregnant</u>
The nuclear medicine doctor will only administer a ^{68}Ga-labelled medicine during pregnancy if a benefit is expected which would outweigh the risks.

<u>If you are breast-feeding</u>
You will be asked to stop breast-feeding. Please ask your nuclear medicine doctor when you can resume breast-feeding.

Driving and using machines
There could be effects on your ability to drive and to use machines due to the use of ^{68}Ga-labelled medicines. Please read the Package Leaflets of these medicines carefully.

3. How gallium (^{68}Ga) chloride solution produced with GalliaPharm is used

There are strict laws on the use, handling, and disposal of radiopharmaceutical products. GalliaPharm will only be used in special controlled areas. The production of gallium (^{68}Ga) chloride solution, radiolabelling of a specific carrier medicine, as well as administration of ^{68}Ga-labelled medicine to you, will only be handled by people who are trained and qualified to use it safely. They will take special care for the safe use of this medicine and will keep you informed of their actions.

The nuclear medicine doctor supervising the procedure will decide on the amount of medicine radiolabelled with ^{68}Ga to be used in your case. It will be the smallest quantity necessary to achieve the appropriate outcome.

Administration of gallium (^{68}Ga) chloride solution and conduct of the procedure
You will not be given the gallium (^{68}Ga) chloride solution, but another medicine which has been combined (radiolabelled) with gallium (^{68}Ga) chloride solution.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure with a ^{68}Ga-labelled medicine. For more information, please read the Package Leaflet of the radiolabelled medicine.

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4. Possible side effects

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Reporting of side effects
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The following information is intended for the specialist only.

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Do not dismantle the case.

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must be used immediately.

6. Contents of the pack and other information

What GalliaPharm contains

- The active substance consists of germanium (^{68}Ge) chloride and gallium (^{68}Ga) chloride dissolved in sterile ultrapure 0.1 mol/l hydrochloric acid. Germanium (^{68}Ge) is irreversibly trapped inside the radionuclide generator decaying to its daughter nuclide (^{68}Ga), which is obtained from the generator as gallium (^{68}Ga) chloride.
- The other ingredients are: Titanium dioxide (matrix)
  Sterile ultrapure 0.1 mol/l hydrochloric acid (solution for elution)

One radionuclide generator is supplied with:

1. 1 x PP – container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid (including a separate hanger for PP-bottles; PP = Polypropylene)
2. 1 x Vented spike (ABS = Acrylonitrile Butadiene Styrene/PE = Polyethylene)
3. 2 x Adapter 1/16" to male LUER (PEEK)
4. 2 x Tubing 60 cm (PEEK)
5. 1 x Tubing 40 cm (PEEK)
6. 1 x Tubing 20 cm (PEEK)
7. 3 x Fingertight fitting 1/16" 10-32 (PEEK)
8. 1 x Fingertight fitting 1/16" M6 (PEEK)
9. 1 x Stopcock manifold (TPX = Polymethylpentene/HDPE = High Density Polyethylene)
10. 1 x Male LUER union (PP)

What GalliaPharm looks like and contents of the pack
You will not need to obtain or handle this medicine.

Marketing Authorisation Holder and Manufacturer
Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

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The following information is intended for healthcare professionals only:

The complete SmPC of GalliaPharm is provided as a separate document in the product package, with the objective to provide healthcare professionals with other additional scientific and practical information about the administration and use of this radiopharmaceutical.

Please refer to the SmPC.

Package leaflet: Information for the patient

GalliaPharm 2.59 GBq radionuclide generator

Gallium (^{68}Ga) chloride solution

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What GalliaPharm is and what it is used for
2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
3. How gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
4. Possible side effects
5. How GalliaPharm is stored
6. Contents of the pack and other information

1. What GalliaPharm is and what it is used for

GalliaPharm is a germanium (^{68}Ge)/gallium (^{68}Ga) radionuclide generator, a device used to obtain a solution of gallium (^{68}Ga) chloride. Gallium (^{68}Ga) chloride is a radioactive substance that is handled by specialised doctors (nuclear medicine doctors) and pharmacists trained to work with radioactive materials. Gallium (^{68}Ga) chloride is not intended for direct use in patients, but is used for radiolabelling, a technique in which a substance is tagged (radiolabelled) with a radioactive compound, here ^{68}Ga.

Only medicines that have been specifically developed and approved for radiolabelling with ^{68}Ga undergo the radiolabelling procedure with gallium (^{68}Ga) chloride. These radiolabelled medicines can recognise and attach to particular types of cells in the body and take the radioactive ^{68}Ga to these cells in your body. The low amount of radioactivity present in the ^{68}Ga-labelled medicine can be detected from outside of the body by special cameras. This may help your doctor with the diagnosis. Please refer to the Package Leaflet of the medicine that is to be radiolabelled with gallium (^{68}Ga) chloride for more information.

The nuclear medicine doctor will explain to you in more detail what type of examination will be performed.

The use of a ^{68}Ga-labelled medicine does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the ^{68}Ga-labelled medicine overcomes the risk due to radiation.

2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must not be used

- if you are allergic to gallium (^{68}Ga) chloride or any of the other ingredients of this medicine (listed in section 6).

If you are using a ^{68}Ga-labelled medicine, you should read information on contraindications in the Package Leaflet of the medicine to be radiolabelled.

Warnings and precautions
For information concerning special warnings and special precautions for use of ^{68}Ga-labelled medicines please refer to the Package Leaflet of the medicine to be radiolabelled.

Children and adolescents
Please speak to your nuclear medicine doctor if you or your child are under 18 years old.

Other medicines and gallium (^{68}Ga) chloride solution
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines since they may interfere with the interpretation of the images by your doctor.

It is not known whether gallium (^{68}Ga) chloride solution may interact with other medicines as specified studies have not been carried out. You will not receive an injection of gallium (^{68}Ga) chloride, but a medicine radiolabelled with ^{68}Ga.

For information concerning other medicines in combination with the use of ^{68}Ga-labelled medicines, please read the Package Leaflet of the radiolabelled medicine.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your nuclear medicine doctor for advice before you are given ^{68}Ga-labelled medicines.

You must inform the nuclear medicine doctor before the administration of ^{68}Ga-labelled medicines if there is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding.

When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

<u>If you are pregnant</u>
The nuclear medicine doctor will only administer a ^{68}Ga-labelled medicine during pregnancy if a benefit is expected which would outweigh the risks.

<u>If you are breast-feeding</u>
You will be asked to stop breast-feeding. Please ask your nuclear medicine doctor when you can resume breast-feeding.

Driving and using machines
There could be effects on your ability to drive and to use machines due to the use of ^{68}Ga-labelled medicines. Please read the Package Leaflets of these medicines carefully.

3. How gallium (^{68}Ga) chloride solution produced with GalliaPharm is used

There are strict laws on the use, handling, and disposal of radiopharmaceutical products. GalliaPharm will only be used in special controlled areas. The production of gallium (^{68}Ga) chloride solution, radiolabelling of a specific carrier medicine, as well as administration of ^{68}Ga-labelled medicine to you, will only be handled by people who are trained and qualified to use it safely. They will take special care for the safe use of this medicine and will keep you informed of their actions.

The nuclear medicine doctor supervising the procedure will decide on the amount of medicine radiolabelled with ^{68}Ga to be used in your case. It will be the smallest quantity necessary to achieve the appropriate outcome.

Administration of gallium (^{68}Ga) chloride solution and conduct of the procedure
You will not be given the gallium (^{68}Ga) chloride solution, but another medicine which has been combined (radiolabelled) with gallium (^{68}Ga) chloride solution.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure with a ^{68}Ga-labelled medicine. For more information, please read the Package Leaflet of the radiolabelled medicine.

After the medicine radiolabelled with gallium (^{68}Ga) chloride solution has been given
The nuclear medicine doctor will inform you if you need to take any special precautions after receiving the ^{68}Ga-labelled medicine. Contact your nuclear medicine doctor if you have any questions.

If you have been given more medicine radiolabelled with gallium (^{68}Ga) chloride solution than you should, or have received direct injection of gallium (^{68}Ga) chloride solution inadvertently
An overdose, or inadvertent direct injection of gallium (^{68}Ga) chloride solution is unlikely, because you will only receive the ^{68}Ga-labelled medicine precisely controlled by the nuclear medicine doctor supervising the procedure. However, in the case of an overdose, or inadvertent direct injection you will receive the appropriate care.

Should you have any further questions on the use of this medicine, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, the ^{68}Ga-labelled medicine can cause side effects, although not everybody gets them.

After the ^{68}Ga-labelled medicine is administered, it will deliver low amounts of ionising radiation with the least risk of cancer and hereditary abnormalities.

For more information about possible side effects, please read the Package Leaflet of the radiolabelled medicine.

Reporting of side effects
If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How GalliaPharm is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

The following information is intended for the specialist only.

The radionuclide generator must not be used after the expiry date stated on the container after "EXP".

Do not dismantle the case.

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must be used immediately.

6. Contents of the pack and other information

What GalliaPharm contains

- The active substance consists of germanium (^{68}Ge) chloride and gallium (^{68}Ga) chloride dissolved in sterile ultrapure 0.1 mol/l hydrochloric acid. Germanium (^{68}Ge) is irreversibly trapped inside the radionuclide generator decaying to its daughter nuclide (^{68}Ga), which is obtained from the generator as gallium (^{68}Ga) chloride.
- The other ingredients are: Titanium dioxide (matrix)
  Sterile ultrapure 0.1 mol/l hydrochloric acid (solution for elution)

One radionuclide generator is supplied with:

1. 1 x PP – container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid (including a separate hanger for PP-bottles; PP = Polypropylene)
2. 1 x Vented spike (ABS = Acrylonitrile Butadiene Styrene/PE = Polyethylene)
3. 2 x Adapter 1/16" to male LUER (PEEK)
4. 2 x Tubing 60 cm (PEEK)
5. 1 x Tubing 40 cm (PEEK)
6. 1 x Tubing 20 cm (PEEK)
7. 3 x Fingertight fitting 1/16" 10-32 (PEEK)
8. 1 x Fingertight fitting 1/16" M6 (PEEK)
9. 1 x Stopcock manifold (TPX = Polymethylpentene/HDPE = High Density Polyethylene)
10. 1 x Male LUER union (PP)

What GalliaPharm looks like and contents of the pack
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Package leaflet: Information for the patient

GalliaPharm 2.96 GBq radionuclide generator

Gallium (^{68}Ga) chloride solution

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What GalliaPharm is and what it is used for
2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
3. How gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
4. Possible side effects
5. How GalliaPharm is stored
6. Contents of the pack and other information

1. What GalliaPharm is and what it is used for

GalliaPharm is a germanium (^{68}Ge)/gallium (^{68}Ga) radionuclide generator, a device used to obtain a solution of gallium (^{68}Ga) chloride. Gallium (^{68}Ga) chloride is a radioactive substance that is handled by specialised doctors (nuclear medicine doctors) and pharmacists trained to work with radioactive materials. Gallium (^{68}Ga) chloride is not intended for direct use in patients, but is used for radiolabelling, a technique in which a substance is tagged (radiolabelled) with a radioactive compound, here ^{68}Ga.

Only medicines that have been specifically developed and approved for radiolabelling with ^{68}Ga undergo the radiolabelling procedure with gallium (^{68}Ga) chloride. These radiolabelled medicines can recognise and attach to particular types of cells in the body and take the radioactive ^{68}Ga to these cells in your body. The low amount of radioactivity present in the ^{68}Ga-labelled medicine can be detected from outside of the body by special cameras. This may help your doctor with the diagnosis. Please refer to the Package Leaflet of the medicine that is to be radiolabelled with gallium (^{68}Ga) chloride for more information.

The nuclear medicine doctor will explain to you in more detail what type of examination will be performed.

The use of a ^{68}Ga-labelled medicine does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the ^{68}Ga-labelled medicine overcomes the risk due to radiation.

2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must not be used

- if you are allergic to gallium (^{68}Ga) chloride or any of the other ingredients of this medicine (listed in section 6).

If you are using a ^{68}Ga-labelled medicine, you should read information on contraindications in the Package Leaflet of the medicine to be radiolabelled.

Warnings and precautions
For information concerning special warnings and special precautions for use of ^{68}Ga-labelled medicines please refer to the Package Leaflet of the medicine to be radiolabelled.

Children and adolescents
Please speak to your nuclear medicine doctor if you or your child are under 18 years old.

Other medicines and gallium (^{68}Ga) chloride solution
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines since they may interfere with the interpretation of the images by your doctor.

It is not known whether gallium (^{68}Ga) chloride solution may interact with other medicines as specified studies have not been carried out. You will not receive an injection of gallium (^{68}Ga) chloride, but a medicine radiolabelled with ^{68}Ga.

For information concerning other medicines in combination with the use of ^{68}Ga-labelled medicines, please read the Package Leaflet of the radiolabelled medicine.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your nuclear medicine doctor for advice before you are given ^{68}Ga-labelled medicines.

You must inform the nuclear medicine doctor before the administration of ^{68}Ga-labelled medicines if there is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding.

When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

<u>If you are pregnant</u>
The nuclear medicine doctor will only administer a ^{68}Ga-labelled medicine during pregnancy if a benefit is expected which would outweigh the risks.

<u>If you are breast-feeding</u>
You will be asked to stop breast-feeding. Please ask your nuclear medicine doctor when you can resume breast-feeding.

Driving and using machines
There could be effects on your ability to drive and to use machines due to the use of ^{68}Ga-labelled medicines. Please read the Package Leaflets of these medicines carefully.

3. How gallium (^{68}Ga) chloride solution produced with GalliaPharm is used

There are strict laws on the use, handling, and disposal of radiopharmaceutical products. GalliaPharm will only be used in special controlled areas. The production of gallium (^{68}Ga) chloride solution, radiolabelling of a specific carrier medicine, as well as administration of ^{68}Ga-labelled medicine to you, will only be handled by people who are trained and qualified to use it safely. They will take special care for the safe use of this medicine and will keep you informed of their actions.

The nuclear medicine doctor supervising the procedure will decide on the amount of medicine radiolabelled with ^{68}Ga to be used in your case. It will be the smallest quantity necessary to achieve the appropriate outcome.

Administration of gallium (^{68}Ga) chloride solution and conduct of the procedure
You will not be given the gallium (^{68}Ga) chloride solution, but another medicine which has been combined (radiolabelled) with gallium (^{68}Ga) chloride solution.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure with a ^{68}Ga-labelled medicine. For more information, please read the Package Leaflet of the radiolabelled medicine.

After the medicine radiolabelled with gallium (^{68}Ga) chloride solution has been given
The nuclear medicine doctor will inform you if you need to take any special precautions after receiving the ^{68}Ga-labelled medicine. Contact your nuclear medicine doctor if you have any questions.

If you have been given more medicine radiolabelled with gallium (^{68}Ga) chloride solution than you should, or have received direct injection of gallium (^{68}Ga) chloride solution inadvertently
An overdose, or inadvertent direct injection of gallium (^{68}Ga) chloride solution is unlikely, because you will only receive the ^{68}Ga-labelled medicine precisely controlled by the nuclear medicine doctor supervising the procedure. However, in the case of an overdose, or inadvertent direct injection you will receive the appropriate care.

Should you have any further questions on the use of this medicine, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, the ^{68}Ga-labelled medicine can cause side effects, although not everybody gets them.

After the ^{68}Ga-labelled medicine is administered, it will deliver low amounts of ionising radiation with the least risk of cancer and hereditary abnormalities.

For more information about possible side effects, please read the Package Leaflet of the radiolabelled medicine.

Reporting of side effects
If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How GalliaPharm is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

The following information is intended for the specialist only.

The radionuclide generator must not be used after the expiry date stated on the container after "EXP".

Do not dismantle the case.

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must be used immediately.

6. Contents of the pack and other information

What GalliaPharm contains

- The active substance consists of germanium (^{68}Ge) chloride and gallium (^{68}Ga) chloride dissolved in sterile ultrapure 0.1 mol/l hydrochloric acid. Germanium (^{68}Ge) is irreversibly trapped inside the radionuclide generator decaying to its daughter nuclide (^{68}Ga), which is obtained from the generator as gallium (^{68}Ga) chloride.
- The other ingredients are: Titanium dioxide (matrix)
  Sterile ultrapure 0.1 mol/l hydrochloric acid (solution for elution)

One radionuclide generator is supplied with:

1. 1 x PP – container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid (including a separate hanger for PP-bottles; PP = Polypropylene)
2. 1 x Vented spike (ABS = Acrylonitrile Butadiene Styrene/PE = Polyethylene)
3. 2 x Adapter 1/16" to male LUER (PEEK)
4. 2 x Tubing 60 cm (PEEK)
5. 1 x Tubing 40 cm (PEEK)
6. 1 x Tubing 20 cm (PEEK)
7. 3 x Fingertight fitting 1/16" 10-32 (PEEK)
8. 1 x Fingertight fitting 1/16" M6 (PEEK)
9. 1 x Stopcock manifold (TPX = Polymethylpentene/HDPE = High Density Polyethylene)
10. 1 x Male LUER union (PP)

What GalliaPharm looks like and contents of the pack
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Marketing Authorisation Holder and Manufacturer
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Robert-Rössle-Str. 10
13125 Berlin
Germany

This leaflet was last revised in.

Other sources of information

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Please refer to the SmPC.

Package leaflet: Information for the patient

GalliaPharm 3.33 GBq radionuclide generator

Gallium (^{68}Ga) chloride solution

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What GalliaPharm is and what it is used for
2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
3. How gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
4. Possible side effects
5. How GalliaPharm is stored
6. Contents of the pack and other information

1. What GalliaPharm is and what it is used for

GalliaPharm is a germanium (^{68}Ge)/gallium (^{68}Ga) radionuclide generator, a device used to obtain a solution of gallium (^{68}Ga) chloride. Gallium (^{68}Ga) chloride is a radioactive substance that is handled by specialised doctors (nuclear medicine doctors) and pharmacists trained to work with radioactive materials. Gallium (^{68}Ga) chloride is not intended for direct use in patients, but is used for radiolabelling, a technique in which a substance is tagged (radiolabelled) with a radioactive compound, here ^{68}Ga.

Only medicines that have been specifically developed and approved for radiolabelling with ^{68}Ga undergo the radiolabelling procedure with gallium (^{68}Ga) chloride. These radiolabelled medicines can recognise and attach to particular types of cells in the body and take the radioactive ^{68}Ga to these cells in your body. The low amount of radioactivity present in the ^{68}Ga-labelled medicine can be detected from outside of the body by special cameras. This may help your doctor with the diagnosis. Please refer to the Package Leaflet of the medicine that is to be radiolabelled with gallium (^{68}Ga) chloride for more information.

The nuclear medicine doctor will explain to you in more detail what type of examination will be performed.

The use of a ^{68}Ga-labelled medicine does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the ^{68}Ga-labelled medicine overcomes the risk due to radiation.

2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must not be used

- if you are allergic to gallium (^{68}Ga) chloride or any of the other ingredients of this medicine (listed in section 6).

If you are using a ^{68}Ga-labelled medicine, you should read information on contraindications in the Package Leaflet of the medicine to be radiolabelled.

Warnings and precautions
For information concerning special warnings and special precautions for use of ^{68}Ga-labelled medicines please refer to the Package Leaflet of the medicine to be radiolabelled.

Children and adolescents
Please speak to your nuclear medicine doctor if you or your child are under 18 years old.

Other medicines and gallium (^{68}Ga) chloride solution
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When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

<u>If you are pregnant</u>
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<u>If you are breast-feeding</u>
You will be asked to stop breast-feeding. Please ask your nuclear medicine doctor when you can resume breast-feeding.

Driving and using machines
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3. How gallium (^{68}Ga) chloride solution produced with GalliaPharm is used

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The nuclear medicine doctor supervising the procedure will decide on the amount of medicine radiolabelled with ^{68}Ga to be used in your case. It will be the smallest quantity necessary to achieve the appropriate outcome.

Administration of gallium (^{68}Ga) chloride solution and conduct of the procedure
You will not be given the gallium (^{68}Ga) chloride solution, but another medicine which has been combined (radiolabelled) with gallium (^{68}Ga) chloride solution.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure with a ^{68}Ga-labelled medicine. For more information, please read the Package Leaflet of the radiolabelled medicine.

After the medicine radiolabelled with gallium (^{68}Ga) chloride solution has been given
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6. Contents of the pack and other information

What GalliaPharm contains

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Please refer to the SmPC.

Package leaflet: Information for the patient

GalliaPharm 3.70 GBq radionuclide generator

Gallium (^{68}Ga) chloride solution

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What GalliaPharm is and what it is used for
2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
3. How gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used
4. Possible side effects
5. How GalliaPharm is stored
6. Contents of the pack and other information

1. What GalliaPharm is and what it is used for

GalliaPharm is a germanium (^{68}Ge)/gallium (^{68}Ga) radionuclide generator, a device used to obtain a solution of gallium (^{68}Ga) chloride. Gallium (^{68}Ga) chloride is a radioactive substance that is handled by specialised doctors (nuclear medicine doctors) and pharmacists trained to work with radioactive materials. Gallium (^{68}Ga) chloride is not intended for direct use in patients, but is used for radiolabelling, a technique in which a substance is tagged (radiolabelled) with a radioactive compound, here ^{68}Ga.

Only medicines that have been specifically developed and approved for radiolabelling with ^{68}Ga undergo the radiolabelling procedure with gallium (^{68}Ga) chloride. These radiolabelled medicines can recognise and attach to particular types of cells in the body and take the radioactive ^{68}Ga to these cells in your body. The low amount of radioactivity present in the ^{68}Ga-labelled medicine can be detected from outside of the body by special cameras. This may help your doctor with the diagnosis. Please refer to the Package Leaflet of the medicine that is to be radiolabelled with gallium (^{68}Ga) chloride for more information.

The nuclear medicine doctor will explain to you in more detail what type of examination will be performed.

The use of a ^{68}Ga-labelled medicine does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the ^{68}Ga-labelled medicine overcomes the risk due to radiation.

2. What you need to know before the gallium (^{68}Ga) chloride solution obtained with GalliaPharm is used

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must not be used

- if you are allergic to gallium (^{68}Ga) chloride or any of the other ingredients of this medicine (listed in section 6).

If you are using a ^{68}Ga-labelled medicine, you should read information on contraindications in the Package Leaflet of the medicine to be radiolabelled.

Warnings and precautions
For information concerning special warnings and special precautions for use of ^{68}Ga-labelled medicines please refer to the Package Leaflet of the medicine to be radiolabelled.

Children and adolescents
Please speak to your nuclear medicine doctor if you or your child are under 18 years old.

Other medicines and gallium (^{68}Ga) chloride solution
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines since they may interfere with the interpretation of the images by your doctor.

It is not known whether gallium (^{68}Ga) chloride solution may interact with other medicines as specified studies have not been carried out. You will not receive an injection of gallium (^{68}Ga) chloride, but a medicine radiolabelled with ^{68}Ga.

For information concerning other medicines in combination with the use of ^{68}Ga-labelled medicines, please read the Package Leaflet of the radiolabelled medicine.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your nuclear medicine doctor for advice before you are given ^{68}Ga-labelled medicines.

You must inform the nuclear medicine doctor before the administration of ^{68}Ga-labelled medicines if there is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding.

When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

<u>If you are pregnant</u>
The nuclear medicine doctor will only administer a ^{68}Ga-labelled medicine during pregnancy if a benefit is expected which would outweigh the risks.

<u>If you are breast-feeding</u>
You will be asked to stop breast-feeding. Please ask your nuclear medicine doctor when you can resume breast-feeding.

Driving and using machines
There could be effects on your ability to drive and to use machines due to the use of ^{68}Ga-labelled medicines. Please read the Package Leaflets of these medicines carefully.

3. How gallium (^{68}Ga) chloride solution produced with GalliaPharm is used

There are strict laws on the use, handling, and disposal of radiopharmaceutical products. GalliaPharm will only be used in special controlled areas. The production of gallium (^{68}Ga) chloride solution, radiolabelling of a specific carrier medicine, as well as administration of ^{68}Ga-labelled medicine to you, will only be handled by people who are trained and qualified to use it safely. They will take special care for the safe use of this medicine and will keep you informed of their actions.

The nuclear medicine doctor supervising the procedure will decide on the amount of medicine radiolabelled with ^{68}Ga to be used in your case. It will be the smallest quantity necessary to achieve the appropriate outcome.

Administration of gallium (^{68}Ga) chloride solution and conduct of the procedure
You will not be given the gallium (^{68}Ga) chloride solution, but another medicine which has been combined (radiolabelled) with gallium (^{68}Ga) chloride solution.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure with a ^{68}Ga-labelled medicine. For more information, please read the Package Leaflet of the radiolabelled medicine.

After the medicine radiolabelled with gallium (^{68}Ga) chloride solution has been given
The nuclear medicine doctor will inform you if you need to take any special precautions after receiving the ^{68}Ga-labelled medicine. Contact your nuclear medicine doctor if you have any questions.

If you have been given more medicine radiolabelled with gallium (^{68}Ga) chloride solution than you should, or have received direct injection of gallium (^{68}Ga) chloride solution inadvertently
An overdose, or inadvertent direct injection of gallium (^{68}Ga) chloride solution is unlikely, because you will only receive the ^{68}Ga-labelled medicine precisely controlled by the nuclear medicine doctor supervising the procedure. However, in the case of an overdose, or inadvertent direct injection you will receive the appropriate care.

Should you have any further questions on the use of this medicine, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, the ^{68}Ga-labelled medicine can cause side effects, although not everybody gets them.

After the ^{68}Ga-labelled medicine is administered, it will deliver low amounts of ionising radiation with the least risk of cancer and hereditary abnormalities.

For more information about possible side effects, please read the Package Leaflet of the radiolabelled medicine.

Reporting of side effects
If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How GalliaPharm is stored

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

The following information is intended for the specialist only.

The radionuclide generator must not be used after the expiry date stated on the container after "EXP".

Do not dismantle the case.

The gallium (^{68}Ga) chloride solution obtained with GalliaPharm must be used immediately.

6. Contents of the pack and other information

What GalliaPharm contains

- The active substance consists of germanium (^{68}Ge) chloride and gallium (^{68}Ga) chloride dissolved in sterile ultrapure 0.1 mol/l hydrochloric acid. Germanium (^{68}Ge) is irreversibly trapped inside the radionuclide generator decaying to its daughter nuclide (^{68}Ga), which is obtained from the generator as gallium (^{68}Ga) chloride.
- The other ingredients are: Titanium dioxide (matrix)
  Sterile ultrapure 0.1 mol/l hydrochloric acid (solution for elution)

One radionuclide generator is supplied with:

1. 1 x PP – container with the eluent, 250 ml sterile ultrapure 0.1 mol/l hydrochloric acid (including a separate hanger for PP-bottles; PP = Polypropylene)
2. 1 x Vented spike (ABS = Acrylonitrile Butadiene Styrene/PE = Polyethylene)
3. 2 x Adapter 1/16" to male LUER (PEEK)
4. 2 x Tubing 60 cm (PEEK)
5. 1 x Tubing 40 cm (PEEK)
6. 1 x Tubing 20 cm (PEEK)
7. 3 x Fingertight fitting 1/16" 10-32 (PEEK)
8. 1 x Fingertight fitting 1/16" M6 (PEEK)
9. 1 x Stopcock manifold (TPX = Polymethylpentene/HDPE = High Density Polyethylene)
10. 1 x Male LUER union (PP)

What GalliaPharm looks like and contents of the pack
You will not need to obtain or handle this medicine.

Marketing Authorisation Holder and Manufacturer
Eckert & Ziegler Radiopharma GmbH
Robert-Rössle-Str. 10
13125 Berlin
Germany

This leaflet was last revised in.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

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Please refer to the SmPC.

販売名	ガリアファーム $^{68}Ge/^{68}Ga$ ジェネレータ	[メジテック]	[ウルトラテクネカウ]
一般名	無 放射性医薬品基準　ガリウム（^{68}Ga）ジェネレータ	無 放射性医薬品基準　過テクネチウム酸ナトリウム（^{99m}Tc）注射液ジェネレータ	無 放射性医薬品基準　過テクネチウム酸ナトリウム（^{99m}Tc）ジェネレータ
会社名	Eckert & Ziegler Radiopharma GmbH （選任外国製造医薬品等製造販売業者：ノバルティスファーマ株式会社）	日本メジフィジックス株式会社	PDR ファーマ株式会社
効能又は効果	陽電子放出断層撮影（PET）イメージングのために承認された被標識用製剤のガリウム（^{68}Ga）標識	○脳腫瘍及び脳血管障害の診断 ○甲状腺疾患の診断 ○唾液腺疾患の診断 ○異所性胃粘膜疾患の診断	○脳腫瘍及び脳血管障害の診断 ○甲状腺疾患の診断 ○唾液腺疾患の診断 ○異所性胃粘膜疾患の診断 ○医療機器「テクネガス発生装置」との組合せ使用による局所肺換気機能の検査
添付文書改訂日	－	2022 年 3 月	2023 年 4 月

2022年3月改訂（第1版）

貯法：室温保存
有効期間：検定日時より12日間

日本標準商品分類番号	
874300	
承認番号	15900AMZ00641000
販売開始	1987年10月

放射性医薬品・脳，甲状腺，唾液腺及び異所性胃粘膜疾患診断薬

放射性医薬品基準過テクネチウム酸ナトリウム（^{99m}Tc）注射液ジェネレータ

処方箋医薬品注)

メジテック®

MEDITEC® Generator

注）注意－医師等の処方箋により使用すること

®：登録商標

3. 組成・性状

3.1 組成

本品は，モリブデン酸塩（^{99}Mo）をガラスカラムに充てんしたアルミナに吸着させ，これに過テクネチウム酸ナトリウム（^{99m}Tc）注射液を溶出させるために必要な装置及び不必要な被曝を避けるための十分なしゃへい装置を合わせたものである。本品中のモリブデン-99とテクネチウム-99mが放射平衡にあるとき，本品のカラムに日局生理食塩液を通じることにより，検定日時において，それぞれ表示される量の過テクネチウム酸ナトリウム（^{99m}Tc）注射液を溶出することができる。

販売名	メジテック	
有効成分	ジェネレータユニット1個中 過テクネチウム酸ナトリウム（^{99m}Tc）（検定日時において） 1.85GBq	ジェネレータユニット1個中 過テクネチウム酸ナトリウム（^{99m}Tc）（検定日時において） 2.78GBq
有効成分	ジェネレータユニット1個中 過テクネチウム酸ナトリウム（^{99m}Tc）（検定日時において） 3.7GBq	ジェネレータユニット1個中 過テクネチウム酸ナトリウム（^{99m}Tc）（検定日時において） 5.55GBq
有効成分	ジェネレータユニット1個中 過テクネチウム酸ナトリウム（^{99m}Tc）（検定日時において） 7.4GBq	ジェネレータユニット1個中 過テクネチウム酸ナトリウム（^{99m}Tc）（検定日時において） 11.1GBq

構成品	本品は次のものから構成され成る。 ・ジェネレータユニット 1個（各包装単位共） ・バイアル入り日局生理食塩液 5mL 5バイアル（各包装単位共） 10mL又は15mL 応需（必要に応じ組み合わせて添付） ・コレクションバイアル（減圧） 5mL用 5バイアル（各包装単位共） 10-15mL用 応需（必要に応じ組み合わせて添付） ・溶出用ニードルガードバイアル 1バイアル（各包装単位共）（溶出液流出ニードル側針カバーに装着済） ・コレクションバイアル用鉛シールド 1個（各包装単位共）（初回のみ送付）

3.2 製剤の性状

販売名	メジテック
本品の使用方法により，本品から溶出した過テクネチウム酸ナトリウム（^{99m}Tc）注射液は次のとおり	
外観	無色澄明の液
pH	4.5～7.0
浸透圧比	約1（生理食塩液に対する比）

4. 効能又は効果

○脳腫瘍及び脳血管障害の診断
○甲状腺疾患の診断
○唾液腺疾患の診断
○異所性胃粘膜疾患の診断

6. 用法及び用量

・溶出法

Ⅰ 溶出操作

(1) バイアル入り日局生理食塩液の装着

バイアル入り日局生理食塩液のゴム栓を日局消毒用エタノールで拭き，針カバーを取り除いた生理食塩液流入ニードルにしっかりとさしこむ。

(2) コレクションバイアルの装着

1) コレクションバイアルをコレクションバイアル用鉛シールドに入れる。

2) コレクションバイアルのゴム栓を日局消毒用エタノールで拭き，針カバーを取り除いた溶出液流出ニードルにさしこむ。

以上の操作により溶出が始まり，30～90秒で溶出は完了する。溶出後は，速やかに次の処置をしておく。

Ⅱ 溶出後の処置

溶出用ニードルガードバイアルのゴム栓（溶出液流出ニードル側針カバーの中央のゴム栓）を日局消毒用エタノールで拭き，コレクションバイアルをはずして溶出液流出ニードルにさしこむ。

注意：空になった生理食塩液のバイアルは，次回の溶出まで取りはずさない。

Ⅲ 再溶出

空の生理食塩液のバイアルをはずし，新しいバイアル入り日局生理食塩液のゴム栓を日局消毒用エタノールで拭き，生理食塩液流入ニードルにさしこむ。その後，溶出用ニードルガードバイアル（溶出液流出ニードル側針カバー）をはずし，前述の「Ⅰ 溶出操作 (2)」と同様にして溶出する。

・投与法

〈脳シンチグラフィ〉

通常，成人には 74～740MBq を静注し，静注後 10～30 分までに（やむを得ず経口投与の場合は 1～2 時間後に）被検部のシンチグラムを得る。

〈甲状腺シンチグラフィ／甲状腺摂取率測定〉

通常，成人には 74～370MBq を静注し，静注後被検部のシンチグラムを得る。同時に甲状腺摂取率を測定する場合には，投与量のカウントと被検部のカウントの比から甲状腺摂取率を測定する。また，7.4～74MBq を静注することにより，甲状腺摂取率のみを測定することもできる。

〈唾液腺シンチグラフィ／RI シアログラフィ〉

通常，成人には 185～555MBq を静注し，静注後被検部のシンチグラムを得る。必要に応じ，唾液分泌刺激物による負荷を行い，負荷後のシンチグラムを得る。また，時間放射能曲線を作成することにより，RI シアログラムを得ることもできる。

〈異所性胃粘膜シンチグラフィ〉

通常，成人には 185～370MBq を静注し，静注後被検部のシンチグラムを得る。

投与量は，年齢，体重により適宜増減する。

8. 重要な基本的注意

診断上の有益性が被曝による不利益を上回ると判断される場合にのみ投与することとし，投与量は最小限度にとどめること。

9. 特定の背景を有する患者に関する注意

9.5 妊婦

妊婦又は妊娠している可能性のある女性には，診断上の有益性が被曝による不利益を上回ると判断される場合にのみ投与すること。

9.6 授乳婦

診断上の有益性及び母乳栄養の有益性を考慮し，授乳の継続又は中止を検討すること。授乳中の女性は投与後少なくとも 3 日間は授乳しない方が良いとの報告がある[1]。

9.7 小児等

小児等を対象とした臨床試験は実施していない。

9.8 高齢者

患者の状態を十分に観察しながら慎重に投与すること。一般に生理機能が低下している。

14. 適用上の注意

〈効能共通〉

14.1 薬剤投与時の注意

膀胱部の被曝を軽減させるため，撮像前後できるだけ患者に水分を摂取させ，排尿させること。

〈脳シンチグラフィ〉

14.2 診断上の注意

脳シンチグラフィを行う場合，脳底部及び後頭蓋窩の腫瘍については，シンチグラム読影が困難な場合がある。

16. 薬物動態

16.3 分布

16.3.1 過テクネチウム酸（$^{99m}TcO_4^-$）は静脈内投与後，速やかに血中から消失し，甲状腺，唾液腺及び胃粘膜に特異的に集積する。その後，腎から尿へ及び腸から糞への 2 つのルートで体外へ排泄される[2,3]。

16.3.2 吸収線量

MIRD 法により算出した吸収線量は次のとおりである[4]。

	吸収線量（mGy/37MBq）
全身	0.11
甲状腺	1.3
胃	0.51
大腸上部	1.2
大腸下部	1.1
膀胱壁	0.85
赤色骨髄	0.17
卵巣	0.30
精巣	0.09

吸収線量値は，抑制剤（$NaClO_4$，$KClO_4$，I_2）で前処置されていない被検者の活動時における値である。

16.5 排泄

静脈内投与後 1 日で約 30%が尿中に排泄され，それ以後尿中への排泄はわずかである。一方，その時期から糞中排泄が次第に増えはじめ，投与後 8 日には投与量の約 60%が糞中に排泄される[3]。

17. 臨床成績

17.1 有効性及び安全性に関する試験

本品が有効であるとされている適応症は以下のとおりである[5-10]。

・脳腫瘍及び脳血管障害（髄膜腫，神経膠芽細胞腫，転移性腫瘍，脳動静脈奇形，硬膜下血腫，他）
・甲状腺疾患（甲状腺機能亢進症，び漫性甲状腺腫，結節性甲状腺腫，甲状腺腫瘍，他）
・唾液腺疾患（シェーグレン症候群，唾液腺腫瘍，他）
・異所性胃粘膜疾患（メッケル憩室，他）

18. 薬効薬理

18.1 測定法

本剤の有効成分に含まれる放射性核種から放出される放射線（ガンマ線）が核医学検査装置により計数化又は画像化される。

18.2 集積機序

本品から溶出される過テクネチウム酸（$^{99m}TcO_4^-$）は，血液－脳関門（blood brain barrier：BBB）を通過しないため，過テクネチウム酸（$^{99m}TcO_4^-$）を投与したときの脳シンチグラム像は，健常人では脳実質に放射能の集積がない cold area として描出される。しかし，脳腫瘍のような BBB 障害患者ではこれを通過して腫瘍組織に高濃度に集積するのでその部分が hot spot として描出される[11,12]。また，病巣部における組織血管床の増加，即ち病巣内血液量の増加，腫瘍その他の病的組織内の血管壁の構造と機能の異常による透過性の亢進，病的組織内の細胞外液腔の増大，pinocytosis，carrier transport，passive diffusion，腫瘍細胞などの代謝と関連した能動的な RI の取込み，その他の機構で取り込まれると考えられる[13]。

その他，本品から溶出される過テクネチウム酸（$^{99m}TcO_4^-$）は甲状腺，唾液腺，胃粘膜等にも集積する。

19. 有効成分に関する理化学的知見

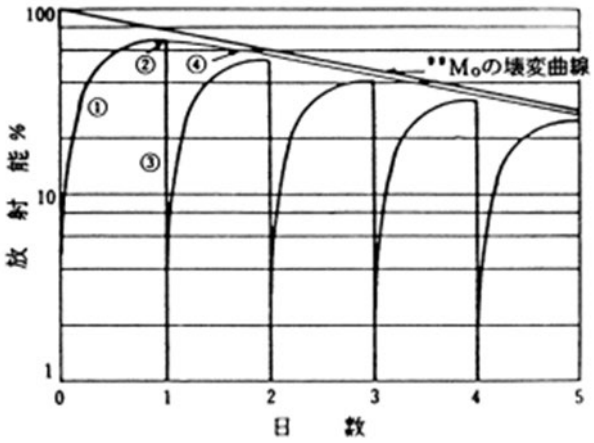
19.1 過テクネチウム酸ナトリウム（^{99m}Tc）

核物理学的特性（^{99m}Tc として）：

・物理的半減期：6.0067 時間

・主γ線エネルギー：141keV（89.1%）

・^{99}Mo の壊変及び ^{99m}Tc の生成



① ^{99}Mo の壊変に伴い ^{99m}Tc が生成する。

② 平衡に達する（^{99m}Tc の最高値）。

③ 生理食塩液で ^{99m}Tc のみ溶出される。

④ 過渡平衡の状態

20. 取扱い上の注意

本剤は，医療法その他の放射線防護に関する法令，関連する告示及び通知等を遵守し，適正に使用すること。

22. 包装

1.85GBq（ジェネレータユニット×1 個），
2.78GBq（ジェネレータユニット×1 個），
3.7GBq（ジェネレータユニット×1 個），
5.55GBq（ジェネレータユニット×1 個），
7.4GBq（ジェネレータユニット×1 個），
11.1GBq（ジェネレータユニット×1 個）

23. 主要文献

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6) 渡辺克司，他：日本医学放射線学会雑誌，1970；30：555-565
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24. 文献請求先及び問い合わせ先

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0120-07-6941（フリーダイヤル）

26. 製造販売業者等

26.1 製造販売元

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参考情報

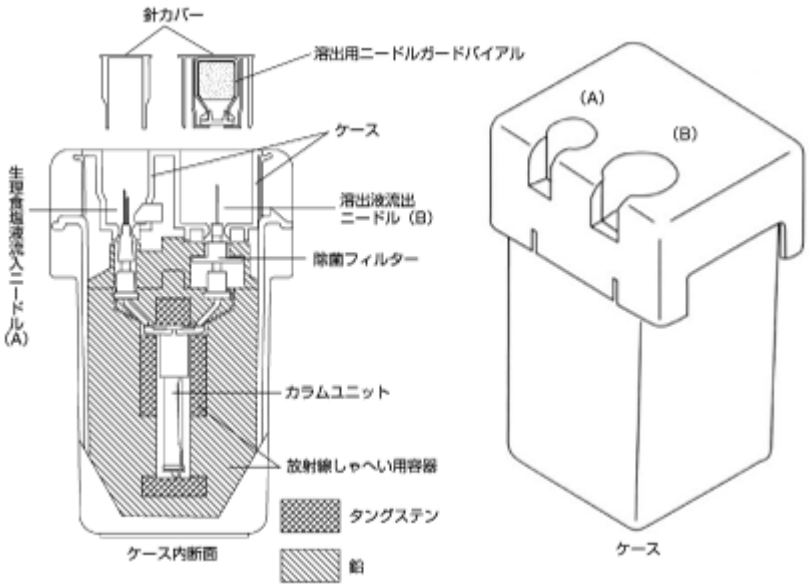


図　ジェネレータユニット

＊＊2023年4月改訂（第3版）
＊2022年3月改訂

日本標準商品分類番号
874300

貯　　法：室温保存
有効期間：検定日から12日間

放射性医薬品／脳・甲状腺・唾液腺及び異所性胃粘膜疾患診断薬・局所肺換気機能診断薬

承認番号	14800AMY00047000
販売開始	1973年3月

処方箋医薬品[注)]

放射性医薬品基準過テクネチウム酸ナトリウム（^{99m}Tc）注射液ジェネレータ

ウルトラテクネカウ®
Ultra-Techne Kow®

注）注意－医師等の処方箋により使用すること

3．組成・性状
＊＊3.1 組成

販売名	ウルトラテクネカウ
有効成分	放射性医薬品基準　過テクネチウム酸ナトリウム（^{99m}Tc）注射液ジェネレータ　1個 表示された日時において溶出されるテクネチウム99mとしてそれぞれ次の放射能を含む。 925MBq　1.85GBq　2.78GBq　3.70GBq　4.63GBq 5.55GBq　7.40GBq　11.1GBq　14.8GBq　18.5GBq
構成品2	日局　生理食塩液 1瓶（200mL）
構成品3	コレクティングバイアル5又はコレクティングバイアル10　8バイアル（必要時16バイアル添付）ガラス製の減圧滅菌バイアル
構成品4	溶出用注射針　8本 外径0.9mm、長さ25mmのディスポーザブル注射針
構成品5	溶出用チューブ　2本（必要時添付） 内径約1mm、長さ5～15cmのシリコン樹脂製チューブの両端に接続具（ポリプロピレン製）を付したもの
構成品6	エリューションシールド　1個（必要時添付）

3.2 製剤の性状

販売名	ウルトラテクネカウ
外観	溶出液（過テクネチウム酸ナトリウム（^{99m}Tc）注射液）：無色澄明の液
pH	溶出液：4.5～7.0
浸透圧比	溶出液：約1（生理食塩液に対する比）

4．効能又は効果
○脳腫瘍及び脳血管障害の診断
○甲状腺疾患の診断
○唾液腺疾患の診断
○異所性胃粘膜疾患の診断
○医療機器「テクネガス発生装置」との組合せ使用による局所肺換気機能の検査

6．用法及び用量
・溶出法
〈脳シンチグラフィ、甲状腺シンチグラフィ/甲状腺摂取率測定、唾液腺シンチグラフィ/RIシアログラフィ、異所性胃粘膜シンチグラフィ〉
透明カバーを取り外し、溶出口に溶出用注射針を取り付ける。コレクティングバイアルをエリューションシールドに入れ、倒立させて溶出口の上からバイアルのゴム栓に溶出用注射針をつけ根まで差し込む。溶出用レバーを用いて溶出回路を開き、バイアル中に溶出液（過テクネチウム酸ナトリウム（^{99m}Tc）注射液）を溶出させる。静置してしばらくすると約5mL、約10mLまたは約20mLの無菌の溶出液が得られる。
〈局所肺換気機能の検査〉
局所肺換気機能の検査（投与法、第5項）のために高い放射能濃度の溶出液を得るときは、次の方法による。
透明カバーを取り外し、溶出口に溶出用チューブの一方を取り付け、他方を容量2～5mLの注射筒に取り付け、溶出液を約2.2mL吸引し、注射筒を取り外して溶出液をコレクティングバイアルに入れる。
溶出用チューブの他方を容量1mLの別の注射筒に取り付け、溶出液を約0.5mL吸引し、注射筒を取り外す。このうち、必要な放射能を医療機器「テクネガス発生装置」に仕込む。
・投与法
〈脳シンチグラフィ〉
通常、成人には74～740MBqを静注し、静注後10～30分までに（やむを得ず経口投与する場合は1～2時間後に）被検部のシンチグラムを得る。
なお、投与量は、年齢、体重によりそれぞれ適宜増減する。
〈甲状腺シンチグラフィ/甲状腺摂取率測定〉
通常、成人には74～370MBqを静注し、静注後被検部のシンチグラムを得る。同時に甲状腺摂取率を測定する場合には、投与量のカウントと被検部のカウントの比から甲状腺摂取率を測定する。また、7.4～74MBqを静注することにより、甲状腺摂取率のみを測定することもできる。
なお、投与量は、年齢、体重によりそれぞれ適宜増減する。
〈唾液腺シンチグラフィ/RIシアログラフィ〉
通常、成人には185～555MBqを静注し、静注後被検部のシンチグラムを得る。必要に応じて唾液分泌刺激物による負荷を行い、負荷後のシンチグラムを得る。また、時間放射能曲線を作成することにより、RIシアログラムを得ることもできる。
なお、投与量は、年齢、体重によりそれぞれ適宜増減する。
〈異所性胃粘膜シンチグラフィ〉
通常、成人には185～370MBqを静注し、静注後被検部のシンチグラムを得る。
なお、投与量は、年齢、体重によりそれぞれ適宜増減する。
〈局所肺換気機能の検査〉
259～370MBq/0.1mLを、医療機器「テクネガス発生装置」に仕込み、その用法及び用量に従って使用する。
^{99m}Tc-超微粒子を発生させたのち、背部よりガンマカメラを用いて観察しながら吸入させ、可能な場合は深吸気を行なわせ、さらに息こらえを行なわせる。
通常、成人には18.5～37MBqを肺内に沈着させ、未沈着の^{99m}Tc-超微粒子を呼出させたのち、肺シンチグラムを得る。
なお、投与量は、年齢、体重によりそれぞれ適宜増減する。

8．重要な基本的注意
診断上の有益性が被曝による不利益を上回ると判断される場合にのみ投与することとし、投与量は最小限度にとどめること。

9．特定の背景を有する患者に関する注意
9.5 妊婦
妊婦又は妊娠している可能性のある女性には、診断上の有益性が被曝による不利益を上回ると判断される場合にのみ投与すること。
9.6 授乳婦
診断上の有益性及び母乳栄養の有益性を考慮し、授乳の継続又は中止を検討すること。授乳中の女性は投与後少なくとも3日間は授乳しない方が良いとの報告がある[1)]。
9.7 小児等
小児等を対象とした臨床試験は実施していない。
9.8 高齢者
患者の状態を十分に観察しながら慎重に投与すること。一般に生理機能が低下している。

11．副作用
次の副作用があらわれることがあるので、観察を十分に行い、異常が認められた場合には適切な処置を行うこと。
11.2 その他の副作用

	頻度不明
過敏症	紅斑性皮疹

14．適用上の注意
14.1 薬剤投与時の注意
〈効能共通〉
14.1.1 膀胱部の被曝を軽減させるため、撮像前後できるだけ患者に水分を摂取させ、排尿させること。
〈局所肺換気機能の検査〉
14.1.2 医療機器「テクネガス発生装置」と組み合わせて用いることによる局所肺換気機能の検査を行う場合、気道抵抗の大きい患者については、安静吸入法を採用すること。また、気道抵抗の大きい患者については呼吸困難に備えて適当な処置法（酸素吸入装置など）を講じておくこと。
〈脳シンチグラフィ〉
14.2 診断上の注意
脳シンチグラフィを行う場合、脳底部及び後頭蓋窩の腫瘍については、シンチグラム読影が困難な場合がある。

16. 薬物動態

16.3 分布

16.3.1 過テクネチウム酸ナトリウム（^{99m}Tc）をラットに静注後、血中の放射能濃度は速やかに減少し、1時間後より胃への放射能の取り込みが見られ、また、3時間後より腎への集積性を示し、この両者は5時間後にピークを示し、その後減少した。医療機器「テクネガス発生装置」との組合わせ使用による^{99m}Tc-超微粒子を吸入させたとき、肺への分布量は全身分布量の91～95%であり、4時間後でも88～92%の範囲であった。肺からの放射能消失速度は、生物学的半減期及び有効半減期がそれぞれ135時間、5.75時間であり、肺での高い滞留性が認められた[2]。

16.3.2 吸収線量

(1)静脈投与

MIRD法により計算した吸収線量は次のとおりである。

臓器	吸収線量（mGy/37MBq）	臓器	吸収線量（mGy/37MBq）
全身	0.14	脾臓	0.11
脳	0.06	胃	2.30
甲状腺	2.35	大腸	1.41
心臓	0.07	腎臓	0.07
肺	0.21	筋肉	0.06
肝臓	0.16	血液	0.44

（自社データ）

(2)局所肺換気機能の検査（医療機器「テクネガス発生装置」との組合せ使用）

MIRD法により計算した吸収線量は次のとおりである。

臓器	吸収線量（mGy/37MBq）	臓器	吸収線量（mGy/37MBq）
甲状腺	0.110	小腸	0.109
肺	3.986	上部大腸	0.085
心臓	0.998	下部大腸	0.073
胃	0.165	腎臓	0.070
肝臓	0.195	睾丸	0.003
脾臓	0.180	膀胱壁	0.053
赤色骨髄	0.154	全身	0.158

（自社データ）

17. 臨床成績

17.1 有効性及び安全性に関する試験

〈脳シンチグラフィ〉

17.1.1 国内臨床試験

脳腫瘍及び脳血管障害患者349例の脳シンチグラフィを行い、あらかじめ臨床的に明らかなもの（レントゲン検査又は手術、剖検により診断の確定したもの）に対し、本剤による診断が適中したものを有効例とした場合の有効率は72.8%（254/349）であった。

〈甲状腺シンチグラフィ/甲状腺摂取率測定、唾液腺シンチグラフィ/RIシアログラフィ、異所性胃粘膜シンチグラフィ〉

17.1.2 国内臨床試験

甲状腺疾患、唾液腺疾患及び異所性胃粘膜疾患患者（112例）に対し本剤による検査を行い、診断に有効な情報が得られたものを有効例とした場合の有効率は次のとおりである。

疾患名	有効率
甲状腺疾患	65/65（100%）
唾液腺疾患	44/45（98%）
異所性胃粘膜疾患	2/2（100%）
合計	111/112（99%）

本剤が投与された112例全例において、本剤に起因すると考えられる臨床症状の変化又は臨床検査値の異常変動はみられなかった。

〈局所肺換気機能の検査〉

17.1.3 国内後期臨床試験

肺気腫、慢性気管支炎、気管支喘息、び漫性汎細気管支炎、肺線維症、過敏性肺炎、肺サルコイドーシス、塵肺症、肺塞栓症、肺梗塞、肺腫瘍、肺炎、肺結核等を含む呼吸器疾患患者（有効性評価対象症例172例）の局所肺換気機能検査を行い、有効な情報が得られたものを有効例とした場合の有効率は97.7%（168/172）であった。

全例（安全性評価対象症例182例）に、テクネガスの投与に起因する自他覚症状、身体所見および臨床検査の変化を認めなかった。

18. 薬効薬理

18.1 測定法

本剤の有効成分に含まれる放射性核種から放出される放射線（ガンマ線）が核医学検査装置により計数化または画像化される。

18.2 集積機序

正常人では過テクネチウム酸イオン$^{99m}TcO_4^-$は、甲状腺、唾液腺、胃粘膜、赤血球、口腔粘膜や筋肉などに集積する。また$^{99m}TcO_4^-$は通常血液脳関門blood brain barrier（B.B.B.）を通過しないため、脳イメージング像は、正常人では脳実質に放射能の集積がない、いわゆるcold areaとして描出され、脳腫瘍のようにB.B.B.に障害のある患者ではこれを通過して腫瘍組織に高濃度に集積するので、その部位がhot spotとして描出される[3]。医療機器「テクネガス発生装置」との組合わせ使用による^{99m}Tc-超微粒子を吸入させたとき、肺での高い滞留性が認められた[2]。

19. 有効成分に関する理化学的知見

19.1 過テクネチウム酸ナトリウム（^{99m}Tc）

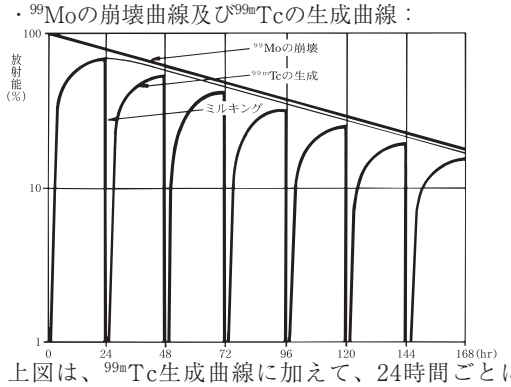
分子式：$Na^{99m}TcO_4$

分子量：185.99

核物理学的特性（^{99}Mo・^{99m}Tcとして）

	^{99}Mo	^{99m}Tc
物理的半減期	65.94時間	6.015時間
主なγ線エネルギー	40.6keV（1.1%） 141keV（82.7%） 181keV（6.0%） 740keV（12.1%） 778keV（4.3%）	141keV（89.1%）

・^{99}Moの崩壊曲線及び^{99m}Tcの生成曲線：



上図は、^{99m}Tc生成曲線に加えて、24時間ごとに生成した^{99m}Tcを生理食塩液を用いて100%ミルキングしたときの溶出パターンも併記してある。ミルキング後^{99m}Tcの放射能は約23時間で最大になり、この時の^{99m}Tcは^{99}Moの約87.7%である（23時間前の^{99}Moの放射能の69%）。

ある時間（t=0）にミルキングを行ない、その後の時間tの^{99m}Tcの放射能（A_T）は、

$$A_T = 0.877A_M \frac{\lambda_T}{\lambda_T - \lambda_M}(e^{-\lambda_M t} - e^{-\lambda_T t})$$

で表わされる。

A_M：^{99}Moの放射能

λ_T：^{99m}Tcの崩壊定数$= \frac{\ln 2}{6.015\text{hr}} \fallingdotseq 0.1152\text{hr}^{-1}$

λ_M：^{99}Moの崩壊定数$= \frac{\ln 2}{65.94\text{hr}} \fallingdotseq 0.0105\text{hr}^{-1}$

t：0時よりの経過時間

・減衰表：

^{99}Mo 物理的半減期 65.94時間		^{99m}Tc 物理的半減期 6.015時間	
経過日数	残存放射能（%）	経過時間	残存放射能（%）
−4	274.3	0	100
−3	213.2	1	89.1
−2	165.6	2	79.4
−1	128.7	3	70.8
0	100	4	63.1
1	77.7	5	56.2
2	60.4	6	50.1
3	46.9	7	44.6
4	36.5	8	39.8
5	28.3	9	35.4
6	22.0	10	31.6
7	17.1	11	28.2
8	13.3	12	25.1
9	10.3	13	22.4
10	8.0	14	19.9
11	6.2	15	17.8
12	4.8	16	15.8

20. 取扱い上の注意

20.1 重量物のため持ち運びには十分注意すること。

20.2 放射線を安全に遮蔽できる貯蔵設備（貯蔵箱）に保存すること。

22. 包装

925MBq［1ジェネレータ］、1.85GBq［1ジェネレータ］、2.78GBq［1ジェネレータ］、3.70GBq［1ジェネレータ］、4.63GBq［1ジェネレータ］、5.55GBq［1ジェネレータ］、7.40GBq［1ジェネレータ］、11.1GBq［1ジェネレータ］、14.8GBq［1ジェネレータ］、18.5GBq［1ジェネレータ］

23．主要文献

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＊24．文献請求先及び問い合わせ先

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電話番号　0120-383-624
〒104-0031　東京都中央区京橋2-14-1　兼松ビルディング

26．製造販売業者等

＊26.1 製造販売元

PDRファーマ株式会社
東京都中央区京橋2-14-1 兼松ビルディング

20XX年X月作成（第１版）

貯法：室温保存
有効期間：検定日より18ヵ月

日本標準商品分類番号
874300

承認番号	XXXXXXXXXX
販売開始	20XX年XX月

放射性医薬品
放射性医薬品基準 ガリウム（^{68}Ga）ジェネレータ

ガリアファーム® ^{68}Ge/^{68}Ga ジェネレータ

GalliaPharm® ^{68}Ge/^{68}Ga Generator

劇薬、処方箋医薬品
（注意－医師等の処方箋により使用すること）

NOVARTIS

3. 組成・性状

3.1 組成

本剤は、ゲルマニウム68を塩化ゲルマニウムの形で、ガラスカラムに充填した二酸化チタンに吸着させ、これに塩化ガリウム（^{68}Ga）溶液を溶出させるために必要な装置及び不必要な被曝を避けるための十分な遮蔽装置を合わせたものである。

販売名	ガリアファーム^{68}Ge/^{68}Gaジェネレータ
有効成分	放射性医薬品基準　ガリウム（^{68}Ga）ジェネレータ　1個 ジェネレータユニット1個中　ゲルマニウム（^{68}Ge）（検定日において）1.85GBq
構成品	本剤は、少なくとも次の個数を含む構成品からなる。 ・　溶出用0.1mol/L塩酸溶液（250 mL）　1個 ・　オスルアーアダプター 1/16”　2個 ・　60cmチューブ　2個 ・　40cmチューブ　1個 ・　20cmチューブ　1個 ・　手締めフィッティング1/16”　10-32　3個 ・　手締めフィッティング1/16”M6　1個 ・　ストップコックマニフォールド　1個 ・　ベントスパイク　1個 ・　オスルアーユニオン　1個

3.2 製剤の性状

販売名	ガリアファーム^{68}Ge/^{68}Gaジェネレータ
本剤の使用方法により、本剤から溶出した塩化ガリウム（^{68}Ga）溶液	
性状	無色澄明の液
pH	0.5～2.0

4. 効能又は効果

陽電子放出断層撮影（PET）イメージングのために承認された被標識用製剤のガリウム（^{68}Ga）標識

6. 用法及び用量

適量の溶出用0.1mol/L塩酸溶液により塩化ガリウム（^{68}Ga）溶液の必要量を溶出し、担体分子の*in vitro*標識に用いる。

7. 用法及び用量に関連する注意

標識に必要な塩化ガリウム（^{68}Ga）溶液の量は、標識する担体分子とその使用目的によって異なるため、被標識用製剤の電子添文を参照すること。

14. 適用上の注意

14.1 薬剤調製時の注意

14.1.1 塩化ガリウム（^{68}Ga）溶液の調製手順の概要（詳細は製造販売業者が提供する調製の手引きを参照すること）

（1）本剤の注入及び溶出ラインを組み立て、溶出用0.1mol/L塩酸溶液と注入ラインを、ジェネレータユニットと注入及び溶出ラインをそれぞれ接続する。

（2）注入ラインに取り付けたシリンジのプランジャーを引き、0.1mol/L塩酸溶液を充填する。なお、充填量は、事前溶出では10mL、^{68}Ga標識のための溶出では5mLとする。

（3）適切なコネクターを使用して溶出ラインを遮蔽容器に接続し、（2）で得られたシリンジ内の0.1mol/L塩酸溶液を2mL/分以下の流速で本剤に注入する。

14.1.2 塩化ガリウム（^{68}Ga）溶液の外観は無色澄明、pHは0.5～2.0、放射化学的純度は95%以上である。外観が無色澄明でない場合は廃棄すること。

14.1.3 塩化ガリウム（^{68}Ga）溶液による被標識用製剤のガリウム（^{68}Ga）標識は微量の金属不純物に影響を受けるため、0.1mol/L塩酸溶液及び溶出液の取扱いに際し、使用する器具の選択には注意すること。

14.1.4 遊離^{68}Geイオンは時間の経過とともにカラムに蓄積するため、本剤を初めて又は96時間以上あけて使用する場合には、^{68}Geの漏出（^{68}Geブレークスルー）レベルの上昇を避けるために、^{68}Ga標識のための溶出前に事前溶出を行うこと。なお、事前溶出の溶出液は廃棄すること。また、^{68}Ga標識のための溶出で得られた塩化ガリウム（^{68}Ga）溶液について、溶出液中の^{68}Gaと^{68}Geの放射能レベルを比較し、^{68}Geの漏出が0.001%以下であることを確認することが望ましい。

14.1.5 塩化ガリウム（^{68}Ga）溶液を患者に直接投与しないこと。誤って投与した場合、投与局所の組織壊死を生じる可能性があるので、誤投与した際はカテーテル又は投与部位を0.9%塩化ナトリウム溶液で洗浄すること。

18. 薬効薬理

18.1 測定法

本剤の有効成分に含まれる放射性核種から放出される放射線（ガンマ線）が核医学検査装置により計数化又は画像化される。

19. 有効成分に関する理化学的知見

核物理学的特性（^{68}Gaとして）

・物理的半減期：67.71分
・主なβ+線エネルギー：1.899MeV(87.94%)、0.822MeV(1.20%)
・主なγ線エネルギー：1.883MeV(0.14%)、1.261MeV(0.09%)、1.077MeV(3.22%)、0.806MeV(0.09%)、0.579MeV(0.03%)、0.511MeV（178.28%）

・減衰表

時間（分）	残存放射能
0	1
15	0.858
30	0.736
60	0.541
90	0.398
120	0.293
180	0.158
360	0.025

20. 取扱い上の注意

20.1 本剤は常温（15～25℃）で使用し、常温以外で保管した場合は、使用前に少なくとも12時間、常温で保管すること。

20.2 本剤は、医療法その他の放射線防護に関する法令、関連する告示及び通知等を遵守し、適正に使用すること。

22. 包装

1.85GBq（ジェネレータユニット×1個）

24. 文献請求先及び問い合わせ先

ノバルティスファーマ株式会社　ノバルティスダイレクト

〒105-6333　東京都港区虎ノ門1-23-1

NOVARTIS DIRECT

0120-003-293

受付時間： 月～金 9：00～17：30

（祝日及び当社休日を除く）

www.novartis.co.jp

26. 製造販売業者等

26.1 選任外国製造医薬品等製造販売業者

ノバルティスファーマ株式会社

東京都港区虎ノ門1-23-1

26.2 外国製造医薬品等特例承認取得者

Eckert & Ziegler Radiopharma GmbH（ドイツ）

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略号一覧

略号	省略していない表現 (英)	省略していない表現 (日)
^{68}Ga	Gallium-68	ガリウム 68
^{68}Ge	Germanium-68	ゲルマニウム 68
DOTA	1,4,7,10-Tetraazacyclododecane-tetraacetic acid	1,4,7,10-テトラアザシクロドデカン-四酢酸
EDTA	ethylenediaminetetraacetic acid	エチレンジアミン四酢酸
PET	positron emission tomography	陽電子放出断層撮影
PSMA	prostate-specific membrane antigen	前立腺特異的膜抗原

1 効能又は効果欄

1.1 効能又は効果

陽電子放出断層撮影（PET）イメージングのために承認された被標識用製剤のガリウム（^{68}Ga）標識

1.2 効能又は効果の設定根拠

ガリアファーム ^{68}Ge/^{68}Ga ジェネレータ｛[Germanium (^{68}Ge) chloride, Gallium (^{68}Ga) chloride] Radionuclide generator，治験成分記号 EZR001, 以下，本剤｝は，有効成分ガリウム（^{68}Ga）を含む塩化ガリウム（^{68}Ga）溶液を溶出するジェネレータ剤である。本剤は，患者に直接投与されることはなく，陽電子放出断層撮影（PET）診断のために， *in vitro* で被標識用製剤へのガリウム（^{68}Ga）標識に使用される。本剤の薬理作用，有効性，及び安全性は，標識に使用される塩化ガリウム（^{68}Ga）ではなく，最終的な標識医薬品の臨床特性のみによって決定される。

本剤の臨床的有用性は，^{68}Ga-PSMA-11 の臨床データ（ロカメッツキットの「2.5 臨床に関する概括評価」に示す）やその他の被標識用製剤を標識した公表文献に基づき確認した。

公表文献については，塩化ガリウム（^{68}Ga）を用いて標識された担体分子の臨床的有用性を検討するため，2022 年 6 月 1 日時点で検索及び評価を行った。その結果，299 件の関連する公表文献が確認された。脳病変に使用された ^{68}Ga-EDTA，神経内分泌腫瘍及び髄膜腫に用いられる ^{68}Ga-DOTA 結合ペプチド，前立腺癌に使用される ^{68}Ga-PSMA-11 について，臨床診断用途に関する ^{68}Ga 標的分子の臨床的有用性が報告されている。

以上より，本剤の効能又は効果を「陽電子放出断層撮影（PET）イメージングのために承認された被標識用製剤のガリウム（^{68}Ga）標識」と設定した。

効能又は効果に関連する注意については，設定不要と考えた。

2 用法及び用量欄

2.1 用法及び用量

標識に必要な塩化ガリウム（^{68}Ga）溶液の量及びその後投与する ^{68}Ga標識医薬品の量は、標識する医薬品とその使用目的によって異なる。標識する個別の医薬品の電子添文を参照すること。

2.2 用法及び用量の設定根拠

本剤は，有効成分ガリウム（^{68}Ga）を含む塩化ガリウム（^{68}Ga）溶液を溶出するジェネレータ剤であり，患者に直接投与しない。本剤の薬理作用，有効性，及び安全性は，標識に使用される塩化ガリウム（^{68}Ga）ではなく，最終的な標識医薬品の臨床特性のみによって決定される。そのため，塩化ガリウム（^{68}Ga）溶液を溶出後，被標識用製剤の電子添文に従って本剤の用法・用量を決定する必要があることから，上記のとおりに設定した。

審査の過程で，医薬品医療機器総合機構との協議を踏まえ，用法及び用量を以下のとおり設定することとした。

適量の溶出用 0.1mol/L 塩酸溶液により塩化ガリウム（^{68}Ga）溶液の必要量を溶出し、担体分子の *in vitro* 標識に用いる。

3 用法及び用量に関連する注意欄

3.1 用法及び用量に関連する注意

7.1 塩化ガリウム（^{68}Ga）溶液を患者に直接投与しないこと。誤って投与した場合、局所の静脈刺激を引き起こし、組織壊死となる可能性がある。カテーテル又は病変部位を0.9%塩化ナトリウム溶液で洗浄すること。

7.2 塩化ガリウム（^{68}Ga）溶液は、様々な担体分子の *in vitro* 標識に用いられる。最終的な医薬品の投与経路を遵守すること。

7.3 本品の使用手順の詳細は、製造販売業者が提供するマニュアル等を参照すること。

3.2 用法及び用量に関連する注意の設定根拠

本剤は，有効成分ガリウム（^{68}Ga）を含む塩化ガリウム（^{68}Ga）溶液を溶出するジェネレータ剤であり，患者に直接投与しない。そのため，用法及び用量に関連する注意として，「塩化ガリウム（^{68}Ga）溶液を患者に直接投与しないこと」を設定し，誤って投与した場合の処置を設定した。

また，本剤の薬理作用，有効性，及び安全性は，最終的な標識医薬品の臨床特性のみによって決定されるため，最終的な医薬品の投与経路を遵守することと注意喚起を設定した。さらに，本剤の詳細な使用手順について別途マニュアルを作成しているため，それを参照することと注意喚起を設定した。

審査の過程で，医薬品医療機器総合機構との協議を踏まえ，用法及び用量に関連する注意を以下のとおり設定することとした。

標識に必要な塩化ガリウム（^{68}Ga）溶液の量は、標識する担体分子とその使用目的によって異なるため、被標識用製剤の電子添文を参照すること。

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14. 適用上の注意欄 3

14. 適用上の注意欄

14. 適用上の注意

14.1 薬剤調製時の注意

14.1.1 塩化ガリウム（^{68}Ga）溶液の調製手順の概要（詳細は製造販売業者が提供する調製の手引きを参照すること）

（1）本剤の注入及び溶出ラインを組み立て、溶出用 0.1mol/L 塩酸溶液と注入ラインを、ジェネレータユニットと注入及び溶出ラインをそれぞれ接続する。

（2）注入ラインに取り付けたシリンジのプランジャーを引き、0.1mol/L塩酸溶液を充填する。なお、充填量は、事前溶出では 10mL、^{68}Ga 標識のための溶出では 5mL とする。

（3）適切なコネクターを使用して溶出ラインを遮蔽容器に接続し、（2）で得られたシリンジ内の 0.1mol/L 塩酸溶液を 2mL/分以下の流速で本剤に注入する。

14.1.2 塩化ガリウム（^{68}Ga）溶液の外観は無色澄明、pH は 0.5～2.0、放射化学的純度は 95%以上である。外観が無色澄明でない場合は廃棄すること。

14.1.3 塩化ガリウム（^{68}Ga）溶液による被標識用製剤のガリウム（^{68}Ga）標識は微量の金属不純物に影響を受けるため、0.1mol/L 塩酸溶液及び溶出液の取扱いに際し、使用する器具の選択には注意すること。

14.1.4 遊離 ^{68}Ge イオンは時間の経過とともにカラムに蓄積するため、本剤を初めて又は 96 時間以上あけて使用する場合には、^{68}Ge の漏出（^{68}Ge ブレークスルー）レベルの上昇を避けるために、^{68}Ga 標識のための溶出前に事前溶出を行うこと。なお、事前溶出の溶出液は廃棄すること。また、^{68}Ga 標識のための溶出で得られた塩化ガリウム（^{68}Ga）溶液について、溶出液中の ^{68}Ga と ^{68}Ge の放射能レベルを比較し、^{68}Ge の漏出が 0.001%以下であることを確認することが望ましい。

14.1.5 塩化ガリウム（^{68}Ga）溶液を患者に直接投与しないこと。誤って投与した場合、投与局所の組織壊死を生じる可能性があるので、誤投与した際はカテーテル又は投与部位を 0.9%塩化ナトリウム溶液で洗浄すること。

14. 適用上の注意の設定根拠

本剤の臨床試験及び欧州添付文書に基づき設定した。

14.1.1 調製手順の概要を示し，詳細は調製の手引きを参照するよう設定した。

14.1.2 塩化ガリウム（^{68}Ga）溶液の外観に異常が認められた場合は廃棄する必要があるため設定した。

14.1.3 塩化ガリウム（^{68}Ga）溶液による被標識用製剤のガリウム（^{68}Ga）標識は微量の金属不純物に影響を受けるため，使用する器具の選択に注意が必要であることから設定した。

14.1.4 本剤を初めて又は 96 時間あけて使用する場合，カラム中で遊離した ^{68}Ge が経時的に蓄積し，^{68}Ge の漏出は理論的に 0.001%を超えて増加する可能性があるものの，本剤の使用前に事前溶出を行うことにより，本剤の有効期間全体を通してこれを 0.001%以下に管理できることから設定した。

14.1.5 塩化ガリウム（^{68}Ga）溶液を患者に直接投与しないよう注意喚起を設定し，また誤って投与した場合の処置を設定した。

1 International Nonproprietary Names for Pharmaceutical Substances (INN)

INN

該当せず。

IUPAC

[^{68}Ge]Germanium tetrachloride / [^{68}Ga]Gallium trichloride

2 放射性医薬品基準収載名

放射性医薬品基準 （以下，放薬基）第 1 通則 3 条では，「放薬基で「基準名」とは，第 4 医薬品各条に掲げる名称又はその別名をいい，法第 50 条の適用については，これを一般的名称とみなす。」とされている。

本剤の放薬基 （案）における基準名は，「ガリウム（^{68}Ga）ジェネレータ」を予定している。放薬基 （案）は，1.13.1 項に添付した。

放射性医薬品基準収載名 （予定）：ガリウム（^{68}Ga）ジェネレータ

<table>
<tr><td>化学名・別名</td><td>【日本名】ガリウム（^{68}Ga）ジェネレータ
【英名】該当せず（INN）
【化学名】
英名：[^{68}Ge]Germanium tetrachloride / [^{68}Ga]Gallium trichloride</td></tr>
<tr><td>構造式</td><td>該当せず</td></tr>
<tr><td>効能・効果</td><td>陽電子放出断層撮影（PET）イメージングのために承認された被標識用製剤のガリウム（^{68}Ga）標識</td></tr>
<tr><td>用法・用量</td><td>適量の溶出用 0.1mol/L 塩酸溶液により塩化ガリウム（^{68}Ga）溶液の必要量を溶出し、担体分子の in vitro 標識に用いる。</td></tr>
<tr><td>劇薬等の指定</td><td></td></tr>
<tr><td>市販名及び有効成分・分量</td><td>原体：ゲルマニウム（^{68}Ge）／ガリウム（^{68}Ga）
製剤：ガリウム（^{68}Ga）ジェネレータ　1 個
ジェネレータユニット 1 個中 ゲルマニウム（^{68}Ge）（検定日において）1.85GBq</td></tr>
<tr><td>毒性</td><td>本剤での毒性試験は実施されていないため，文献報告に基づき硫酸ガリウム及び不活性硝酸ガリウムの毒性情報を記載した。

単回投与毒性試験（乳酸ガリウムを用いた文献報告より）
<table>
<tr><td>概略の致死量 (mg/kg)</td><td>静脈内</td></tr>
<tr><td>ラット</td><td>46 mg/kg</td></tr>
<tr><td>ウサギ</td><td>43 mg/kg</td></tr>
</table>
反復投与毒性試験（不活性硝酸ガリウムを用いた文献報告より）
<table>
<tr><td>動物種</td><td>投与期間</td><td>投与経路</td><td>投与量 (mg/kg)</td><td>無毒性量 (mg/kg)</td><td>主な所見</td></tr>
<tr><td>マウス</td><td>10 日間</td><td>腹腔内</td><td>報告なし</td><td>報告なし</td><td>報告なし
概略の致死量：
80.0 mg/kg</td></tr>
<tr><td>ラット</td><td>10 日間</td><td>腹腔内</td><td>報告なし</td><td>報告なし</td><td>報告なし
概略の致死量：
67.5 mg/kg</td></tr>
</table></td></tr>
<tr><td>副作用</td><td>本剤で標識した医薬品の電子添文を参照すること。</td></tr>
<tr><td>会社</td><td>Eckert & Ziegler Radiopharma GmbH
（選任外国製造医薬品等製造販売業者：ノバルティスファーマ株式会社）
製剤：輸入</td></tr>
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4.3 参考文献 （評価／参考の別：参考資料）		
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3 第 5 部

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考	電子データの提出
5.2 全臨床試験一覧表							
－	－	該当資料なし	－	－	－	－	－
5.3 臨床試験報告書							
5.3.1 生物薬剤学試験報告書							
5.3.1.1 バイオアベイラビリティ（BA）試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.1.2 比較 BA 試験及び生物学的同等性（BE）試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.1.3 In Vitro-In Vivo の関連を検討した試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.1.4 生物学的及び理化学的分析法検討報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.2 ヒト生体試料を用いた薬物動態関連の試験報告書							
5.3.2.1 血漿蛋白結合試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.2.2 肝代謝及び薬物相互作用試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.2.3 他のヒト生体試料を用いた試験報告書							
－	－	該当資料なし	－	－	－	－	－

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考	電子データの提出
5.3.3 臨床薬物動態（PK）試験報告書							
5.3.3.1 健康被験者における PK 及び初期忍容性試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.3.2 患者における PK 及び初期忍容性試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.3.3 内因性要因を検討した PK 試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.3.4 外因性要因を検討した PK 試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.3.5 ポピュレーション PK 試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.4 臨床薬力学（PD）試験報告書							
5.3.4.1 健康被験者における PD 試験及び PK/PD 試験報告書							
－	－	該当資料なし	－	－	－	－	－
5.3.4.2 患者における PD 試験及び PK/PD 試験報告書							
－	－	該当資料なし	－	－	－	－	－

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考	電子データの提出
5.3.5 有効性及び安全性試験報告書							
5.3.5.1 申請する適応症に関する比較対照試験報告書							
5.3.5.1-1	VISION (CAAA617A12301)-PA 総括報告書		2018 年 5 月～2021 年 1 月	ベルギー，カナダ，デンマーク，フランス，オランダ，スウェーデン，英国，米国，ドイツ	外国	評価	あり
	VISION (CAAA617A12301)-FA 総括報告書		2018 年 5 月～2023 年 12 月	ベルギー，カナダ，デンマーク，フランス，オランダ，スウェーデン，英国，米国，ドイツ	外国	評価	－
	VISION (CAAA617A12301) Imaging Study Report: Reviewer variability					評価	あり
	VISION (CAAA617A12301) Imaging Study Report: Reviewer variability Statistical Methods					－	－
	VISION (CAAA617A12301) Imaging Study Report: Quantitative analysis					参考	－
	VISION (CAAA617A12301) Imaging Study Report: Quantitative analysis errata					－	－
	VISION (CAAA617A12301) Imaging Study Report: Quantitative analysis Statistical Methods					－	－
	VISION (CAAA617A12301) Imaging Study Report: Quantitative analysis Independent Review Charter					－	－

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考	電子データの提出
5.3.5.1-2	PSMAfore (CAAA617B12302) 総括報告書		2021 年 6 月～2024 年 2 月（データカットオフ日） 本報告時点で継続中	オーストリア，ベルギー，カナダ，チェコ，フランス，ドイツ，オランダ，ポーランド，スロバキア，スペイン，スウェーデン，スイス，英国，米国	外国	評価	あり
	PSMAfore (CAAA617B12302) Errata						
	PSMAfore (CAAA617B12302) C1 Kidney Dosimetry Report						
5.3.5.2　非対照試験報告書							
5.3.5.2-1	CAAA617A11201 総括報告書		2022 年 1 月～2023 年 12 月（データカットオフ日） 本報告時点で継続中	日本	国内	評価	あり
5.3.5.3　複数の試験成績を併せて解析した報告書							
5.3.5.3-1	SCS Appendix 1		—	—	—	—	—
	SCS Appendix 1 Errata						
5.3.5.3-2	EU Clinical Overview		—	—	—	—	—
5.3.5.4　その他の臨床試験報告書							
—	該当資料なし		—	—	—	—	—
5.3.6　市販後の使用経験に関する報告書							

添付資料番号	Report No./Study No.	タイトル	試験実施期間	試験実施場所	報種類（国内／外国）	評価／参考	電子データの提出
－	該当資料なし		－	－	－	－	－
5.3.7　患者データ一覧表及び症例記録							
－	該当資料なし		－	－	－	－	－

添付資料番号	著者・タイトル・掲載誌	報種類（国内／外国）
5.4 参考文献 （評価／参考の別：参考資料）		
－	該当資料なし	－